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A.M.A. Session . NEW YORK . June 10-14, 1940

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RENAL TUBERCULOSIS AS A COMMUNITY PROBLEM

CHAIRMAN'S ADDRESS

WILLIAM P. HERBST, M.D.

WASHINGTON, D. C.

This address is dedicated to the prevention of deaths caused by renal tuberculosis. The saving of a life by nonspectacular means is just as valuable economically as one saved by the most brilliant surgical operation. The factors involved in this problem consist of conditions which influence (1) the recognition of the presence of the tubercle bacillus in urine, (2) the general resistance of the individual, (3) the mortality from procedures instituted in treatment and (4) provision of adequate facilities and detailed direction of every individual affected.

RECOGNITION OF THE PRESENCE OF THE BACILLUS

The recognition of the presence of tuberculous involvement of a kidney or kidneys is dependent on urographic evidence of renal tissue destruction and the finding of the tubercle bacillus in urine from the kidney. When to look for the tubercle bacillus is important. The following conditions indicate the advisability of a search: 1. Unilateral renal infection. 2. Hematuria with no obvious explanation. 3. Pyuria with no organisms demonstrable by ordinary staining methods. 4. Persistent pyuria of any kind. 5. Cystitis which does not respond to a reasonable period of treatment. 6. Pyuria or dysuria in individuals with a history of tuberculosis or active extra-urinary tuberculous lesions; nodular lesions in the seminal tract. 7. Urographic evidence of the destruction of renal tissue.

The technic of recognizing the presence of the tubercle bacillus is far from being uniform and is unsatisfactory so far as the cross section of this activity is concerned. It was Dr. Keyes who some years ago compared the percentage of accuracy in finding tubercle bacilli in his private cases as contrasted to those in ward cases. He found that his own percentage was about 90 and that of the ward cases about half the latter figure. Cultural methods have been found to be rather accurate in the hands of a few technicians. Eisendrath in a study of 424 cases of renal tuberculosis found the culture to be positive in nearly all and a smear positive in 351. Of 124 cases which were found in the literature in which the comparison between cultures and guinea pig inoculations was reported, the cultures were found to be positive in sixty-one and the guinea pig inoculations positive in fifty-five cases. The largest number of cases in which the three methods were compared is that of Dimtza (cited by Eisendrath). In eighty-one cases a smear only was positive in fifty-eight, the guinea pig inoculation in seventy-six and cultures in eighty. These figures do not give an accurate picture of the problem as it exists because they are reports of individuals who are much more careful of their work than the average of the profession at large. The common practice in many laboratories in searching for the tubercle bacillus is to accept whatever specimen or specimens are presented to them by the physician and render a report. Unfortunately, in many instances they refrain from embarrassing a physician sending in the specimen by insisting that he send in multiple specimens for staining or, in the case of a specimen for guinea pig inoculation, that he send in not less than three specimens which are to be injected into a pig or pigs. The question of staining methods is very important, but the most important factor is that of experience, which makes the difference between the 90 and the 45 per cent reported by Dr. Keyes. The technical facilities in the nature of cystoscopic facilities is important. In the nation's capital, astounding as it may seem, the newly constructed city tuberculosis sanatoriums for adults and children do not have an equipped cystoscopy room. This is a lamentable situation which should not be allowed to exist in any community.

GENERAL RESISTANCE OF THE INDIVIDUAL

The entity called general resistance is the most important single factor in the whole picture, since it is the handling, consideration and conservation of this factor which ultimately results in recovery or death. The various health department statistics demonstrate the influence of the general resistance factor of the economic status in the extreme preponderance of Negro as compared to white deaths. In the nation's capital the mortality from tuberculosis in all forms is about three times greater in the Negro than in the white race. Renal tuberculosis is supposed to be present in about 5 per cent in all cases of tuberculosis. Thomas found it clinically in 3.87 per cent of the patients admitted to Glen Lake Sanatorium and with additional cases by autopsy making a total of 5.5 per cent. In the city of Detroit, where the tuberculosis problem is supposed to be well handled, we find that the mortality among the Negroes is over six times as great as in the white population. The economic status of any community is a factor which is important but which we as a profession can do little about. We all have seen patients advised of the necessity of long hospitalization refuse because of the responsibility for their dependents, only to return subsequently with a condition which proved to be fatal. Dr. Morris Fishbein explained to the National Health Conference that the economic status of the population was more

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vital than extravagant ideas advised by some at that conference. This was a concrete example of advice on the part of the profession. The profession should go a step further, however, and be constructive, as it can well be in any community, by enlisting cooperative public group pressure, with appropriate publicity, on legislators to appropriate adequately for maintenance of the breadwinner's dependents when they are ill. We can also get behind movements directed toward the elimination of slums, where tuberculosis has its greatest incidence. The matter of climate is important. Dr. W. C. Shultz of Tucson, Ariz., stated: "I rarely find genito-urinary complications in patients who have been residents of Arizona for any period of time." Dr. Don Augusto S. Boyd, ambassador of Panama, who is a prominent surgeon, told me that renal tuberculosis does not exist in Panama though there are many cases of pulmonary tuberculosis. Of course, climatic treatment cannot be applied to the indigent, but it is very important to prescribe a favorable climate for those who can afford it. Ultraviolet radiation and heliotherapy are very valuable in their effect on the general resistance when they are intelligently used, and Wang even employs them intravesically. Two very important precautions should be observed: Ultraviolet radiation is definitely contraindicated in patients with pulmonary tuberculosis and should never be administered to the point where it produces fatigue. Because of failure to observe these simple precautions, many patients have succumbed from overtreatment. The influence of diet on the resistance is also important. The diet should be abundant and well balanced but not forced to the point of gorging. It should be rich in vitamins, and usually it is wise to supplement it with vitamins in concentrated form. The diet should include at least one quart of whole milk daily, taken either at mealtime or between meals (Dr. Charles P. Cake). Rest is highly important, and the patient should not be expected to engage in any strenuous physical activity of any kind after nephrectomy for varying periods ranging from several months to two years, depending on the physical condition. Of course, a patient with active tuberculosis anywhere else in the body must have continuous bed rest. Another important measure in the management of patients with renal tuberculosis who have no open lesion is to be sure that they are not exposed to patients with open lesions in wards. This is not possible in many communities today because of a lack of beds for this type of patient. Some of the health departments have no definite policy in this regard, probably because they have no facilities with which to pursue any policy.

MORTALITY FROM PROCEDURES INSTITUTED IN TREATMENT

There are many variables in this phase of the problem. First of all, the type of tuberculosis of the kidney varies. There are cases in which a single lesion exists and heals spontaneously without being recognized. The number of these is naturally indeterminate. Next there is the chronic form which starts as a minute lesion below the surface of the papillae and progresses very slowly to varying degrees of erosion, cavitation, fibrosis or abscess formations extending throughout and beyond the kidney. In a few of these cases atresia of the ureter occurs with spontaneous autonephrectomy. There is controversy over the so-called tuberculous nephritis which Wildbolz claims exists and Lieberthal and others question. The acute miliary type is a very rapidly developing process which is a part of a general miliary tuberculosis and rapidly fatal. From a practical standpoint the treatment instituted applies to the group of chronic types. Nonoperative treatment presumes that the patient is too gravely ill to withstand surgery or that his response is good and therefore a chance for spontaneous cure exists. The greater number of authorities deny that tuberculosis of the kidney ever heals. Thomas and Medlar champion the view that renal tuberculosis can and does heal. I believe that tuberculosis of the kidney does heal because I have seen at least two cases in which involvement of the remaining kidney after nephrectomy for renal tuberculosis became arrested. What is more important to my mind is the untenability of the position that renal tissue cannot heal when pulmonary, glandular, peritoneal, and other tissues can. Wildbolz reported 316 nonsurgical cases in which 58 per cent of the patients died in five years or less and in which 6 per cent lived more than ten years. He states that only two cases of spontaneous healing had been reported up to 1932. He reports a recovery in 86 per cent of nephrectomized patients when no other lesions existed, and 43 per cent when genital lesions coexisted. Thomas has followed many cases for years under constant observation. All things being equal, the great preponderance of data justifies early nephrectomy, and the earlier the recognition the better the results. In view of the fact that renal tuberculosis does heal, even in rare instances, the postoperative care is most vital. All the factors enumerated under general resistance should be scrupulously observed and employed in order to reduce greatly the ultimate mortality. All authorities agree that the postoperative care is very important. Their policy varies anyway from the giving of general directions to prolonged sanatorium and climatic care, even in cases uncomplicated by active tuberculosis elsewhere. It is my opinion that in the uncomplicated as well as the complicated cases a minimum of a year's constant supervision of the urine should be given and if economically possible I would send everybody to a climatic environment such as Arizona for not less than a year. We must be practical, however, and meet the problem as satisfactorily as we can, striving constantly to improve the economic factors in our own communities.

PROVISION OF ADEQUATE FACILITIES AND DETAILED DIRECTION OF EVERY INDIVIDUAL AFFECTED

The medical society should make a survey including the status of clinical laboratory facilities for the detection of the tubercle bacillus in urine, the resources available for taking care of resistance factors of the indigent and the number and kind of beds available for tuberculous patients. Having done these things, it should urge ample provision of cultural facilities in all private and hospital clinical laboratories, influence the health department to furnish cultural facilities in its laboratories equal to those for diphtheria, meet with and enlist cooperation of all lay organizations and health departments in acquiring public funds for two and one-half beds per death, and carry out social service care of dependents, elimination of slums where tuberculosis is preponderant, and work for general improvement in general standard of living conditions.

On a national scale, the laboratory men, professional tuberculosis societies and urologic groups should standardize cultural and other clinical laboratory investigation methods for the detection of the tubercle bacillus in urine and urge the profession to use them.

Community action on the part of any medical society along these lines will result in some degree in dispelling prevailing public opinion that we are obstructive to their acquisition of cheap or free medical service and, what is more important, will stamp physicians as authoritative, dynamic and sympathetic leaders in solving community health problems.

1801 I Street N.W.

THE TREATMENT OF MASSIVE HEMORRHAGE DUE TO PEPTIC ULCER

JOHN S. LA DUE, M.D.
MINNEAPOLIS

All patients with hematemesis and melena due to peptic ulcer admitted to the Long Island College Hospital are fed immediately and repeatedly. This treatment has been employed in all ward and in a majority of private cases during the last eighteen years.

The therapy was devised by Dr. Andresen [1] in 1916. He first gave gelatin mixtures to patients recovering from a gastro-enterostomy with such favorable results that he decided to give the same mixture to patients with gastric hemorrhage.

Most clinicians advocate a period of fasting, the giving of fluids and transfusions when needed, and rest. Lenhartz [2] in 1906 treated 146 cases of hemorrhage due to peptic ulcer by feeding eggs and milk immediately. The mortality was 2.14 per cent.

Carlson [3] demonstrated that an empty stomach is one in which active peristalsis and secretion take place. After hemorrhage the stomach is empty or filled with blood, usually clotted. The blood with its high protein content acts as a powerful stimulant for the production of gastric juice. A stomach partly filled with food which combines rapidly with any gastric secretion is preferable to an actively contracting stomach full of secretions which are likely to digest the clots plugging the bleeding vessel or even the injured vessel wall itself. Since the purpose of any treatment is primarily the stopping of hemorrhage, it is reasonable to strive to keep the stomach as completely at rest as possible. Equally important is the inactivation of potent gastric secretions.

In 1936 Meulengracht [4] reported a series of 251 cases of severe hematemesis and melena with a mortality of 1 per cent. The patients were fed five times a day on such foods as meat balls, chops, potatoes, vegetable purées and steamed apricots.

Mortalities reported in the literature are summarized in table 1. Cases in which immediate and repeated feedings are given have significantly lower mortalities than those in which a period of starvation is employed. Only six of the twenty investigators who withheld food report a mortality of less than 10 per cent.

In the therapy for bleeding ulcer to be described here there are four objectives: (1) stoppage of bleeding by the formation of clots at the site of hemorrhage; (2) prevention of an increase in blood pressure (already low as a result of hemorrhage) so rapid as to dislodge these clots; (3) management of shock, with avoidance of too much stimulation, which often results in recurring hemorrhage, and (4) prevention of the digestion by gastric secretion of the exposed wound in the blood vessel or of the clots filling the defect.

Rest is essential if any one of these objectives is to be realized. Patients must have absolute rest in bed and be constantly reassured, lest fear and its resultant restlessness upset the entire regimen. They are usually morphinized for twenty-four hours, or longer if necessary.

Intravenous and parenteral fluids are not given as a routine, their desirability being far outweighed by the danger of increasing the blood pressure to a point high enough to dislodge clots already formed. Transfusions are avoided when possible early in the treatment for the same reason but are given in amounts of from 200 to 300 cc. if the systolic blood pressure falls below 90 or the hemoglobin content below 30 per cent. Occasionally one such transfusion will carry a patient past the danger point, but it is again emphasized that transfusions are reserved for the exsanguinated, moribund patient and are not given as a routine. After all signs of hemorrhage have disappeared, large transfusions may materially shorten the period of convalescence.

Stimulants are given rarely and with great caution lest the patient's activity be increased enough to cause another hemorrhage. The surface of the body is kept warm and nothing that might cause chilling, such as the use of ice bags over the epigastrium, is employed.

Emesis, melena and retching, always exhibited in some degree, indicate irritability of the gastrointestinal tract. The diet employed is designed to overcome this irritability and hypersecretion.

Table 2 shows the type and schedule of feedings given to patients with hemorrhage due to peptic ulcer. Four ounces of a gelatin mixture (consisting of 30 Gm. of gelatin, 90 Gm. of lactose, 1,000 cc. of water and the juice of an orange for flavor) is fed every one and a half hours except when the patient is sleeping. On the third day 5 ounces of a gruel mixture (made from 500 Gm. of cereal gruel, 420 Gm. of milk, 120 Gm. of cream and 90 Gm. of lactose) is given every hour and a half in addition to the gelatin. On the fifth and sixth days, 6 ounces of gruel mixture 2 (350 Gm. cereal gruel, 1,000 Gm. of milk, 120 Gm. of cream, 120 Gm. of lactose) with 6 ounces of gelatin solution is fed every hour and a half. A poached egg, custard or jello may be added to the gruel after the fifth day. On the seventh and eighth days, feedings are given every two hours. On the ninth day the Long Island College Hospital ulcer diet, a bland diet given without alkalis, is begun.

As the work of Carlson has shown, an empty stomach is never at rest; it appears desirable to keep the stomach as nearly at rest as possible by keeping it partly full. The diet described is adequate in this respect, is soothing and combines rapidly with any gastric juice that may be present. The gelatin solution lessens the distressing thirst exhibited by these patients and supplies more than 1,000 calories and 2,000 cc. of fluid every twenty-four hours. No amount of reassurance is so effective in quieting the patients' worry as the giving of nourishment so soon after hemorrhage. X-ray films

From the Medical Service of the Long Island College Hospital, Brooklyn.
Read before the Section on Practice of Medicine at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1. Andresen, A. F. R.: The Treatment of Gastric Hemorrhage, J. A. M. A. **89**: 1397 (Oct. 22) 1927.
2. Lenhartz, H.: Ueber die Behandlung des Magengeschwürs, Mitt. a. d. Hamb. Staatskrankenanst **6**: 345, 1906.
3. Carlson, A. J.: The Control of Hunger in Health and Disease, Chicago, The University of Chicago Press, September 1936.
4. Meulengracht, E.: The Treatment of Hematemesis and Melena with Food, Lancet **2**: 1220 (Nov. 30) 1935.

are taken from seven to ten days after bleeding ceases. Hospitalization averages 27.5 days in this series.

In preparation for this report, the gastric hemorrhage cases admitted from 1925 to 1936 inclusive were studied, and only the eighty-two cases that appeared according to all accepted criteria to present genuine ulcers were included.

Seventeen cases failed to reveal evidence of ulcer by x-ray examination, but the gastrointestinal series were made from two to six weeks after signs of bleeding had disappeared and the ulcers had had time to heal. In seven of these cases there were no symptoms prior to hemorrhage; in the other ten there were chronic gastric complaints. Duodenitis was ruled out by fluoroscopic studies.

All patients had had bleeding severe enough to force them to seek hospitalization, and all had bled shortly before entry. Red blood cell counts on admission were less than three million and hemoglobin contents less than 60 per cent. Seventy-six patients exhibited symptoms and physical signs of severe hemorrhage on admission, such as rapid shallow respiration, low blood pressure, syncope and collapse. The remaining six had these symptoms in a lesser degree at some time during their stay in the hospital.

Accepted criteria for hemorrhage from the gastrointestinal tract were hematemesis, melena or both. Of the fifty-four patients found to have duodenal ulcer, two had vomited blood, thirteen had passed tarry stools and thirty-nine had done both. The eleven patients with gastric ulcers both vomited blood and passed tarry stools. Of the eighty-two patients, 75 per cent had a history of hematemesis and melena, 17 per cent of tarry stools alone and 7 per cent of hematemesis alone.

Fifty-eight, or 70 per cent, of these patients were men. Seventy-five per cent were between 30 and 60 years of age. The largest single age group, constituting 30 per cent, was in the 40 to 50 year range. There was a previous history suggestive of ulcer in seventy-two cases (87 per cent), but in ten cases the hemorrhage was the first symptom noted by the patient. In thirty-three cases there was a history of previous hemorrhage.

Gastric analyses were done in forty-nine cases. In twenty-seven an excessive amount of free hydrochloric acid was found and the curve over the two hour period remained elevated; in sixteen approximately normal curves were observed and in five patients (all at least 50 years of age) the acidity was low. The stools gave a positive benzidine reaction for from five to thirty days after entry.

Not one of the patients who died was operated on, and in the two cases in which consent for autopsy was secured the character and site of the lesion precluded any successful surgical procedure, in the opinion of the pathologist, internist and surgeon present at the autopsy.

Table 1.—*Mortality Rates of Hemorrhage Due to Peptic Ulcer*

Author	Place	Number of Cases	Death Rate, Percentage
Treatment by Immediate and Repeated Feedings			
Lenhartz [2]	Not stated	146	2.14
Meulengracht [4]	Copenhagen	251	1.0
Bernstein, B. M.: M. Rec. **144**: 178, 1936	Jewish Hospital, Brooklyn	28	0.0
Treatment by Period of Starvation			
Allen, A. W., and Benedict, E. B.: Ann. Surg. **98**: 736, 1933	Massachusetts General Hospital	138	14.5
Goldman, L.: J. A. M. A. **107**: 1537, 1937	San Francisco General Hospital	349	11.5
Westermann [7]	St. Luke's Hospital, N. Y. C.	50	20.0
Eggleston, E. L.: J. A. M. A. **75**: 1542, 1920	Michigan	95	1.0
Manheim, S. D.: M. J. & Rec. **124**: 98, 1926	Mount Sinai Hospital, N. Y. C.	101	8.9 (total) 4.2 (med.)
Hendon, G. A.: Am. J. Digest. Dis. & Nutrition **2**: 255, 1935	Louisville, Ky.	46	10.0
Hinton [6]	Bellevue Hospital, N. Y. C.	52	20.0
Lynch [9]	Montreal General Hospital	31 (med.) 21 (surg.)	12.9 42.8
Ross, H.: M. J. Australia **1**: 168, 1930	Australia	187	6.5
Aitken, R. S.: Lancet **1**: 839, 1934	London Hospital	255	11.0
Bulmer, E.: Lancet, **2**: 720, 1932	Birmingham, England	578	10.7
Babey, A. M.: Guy's Hosp. Rep **86**: 129, 1936	Guy's Hospital	82	4.8
Burger, G., and Hartfall, J.: ibid **84**: 197, 1934	Guy's Hospital	137	22.0
Conybeare, J. J., and Bolton, C.: Proc. Roy. Soc. Med. **27**: 225, 1934	Guy's Hospital	600	2.5
Chiesman, W. E.: Lancet **2**: 722, 1932	St. Thomas's Hospital	191	25.0
Davies, L., and Nevin, R.: Brit. M. J. **2**: 858, 1934	St. Thomas's Hospital	391	21.0
Gordon-Taylor, G.: Lancet **2**: 811, 1935	Middlesex Hospital	Not stated	21.0
Hellier, F. F., and Camb, M. A.: Lancet **2**: 1271, 1934	Leeds	202	13.0
Cullinan, E. R., and Price, R. K.: St. Bart.'s Rep., 1932, p. 184	St. Bartholomew's Hospital	105	18.1
Paterson, J. H.: Proc. Roy. Soc. Med. **17**: 2, 1924	London	100	4.0

Of the eighty-two patients eight died, seven as a direct result of repeated hemorrhage. Three of these fatalities are not included in the mortality statistics because one patient died of pneumonia contracted six weeks after entry when the hemorrhage had been well controlled; one died in the accident room before treatment could be administered and one was not given feedings. Hence the mortality is 6.3 per cent.

One patient lived eight days after admission, the others an average of twenty-six hours after the onset of their hemorrhage. The fatalities, with one exception, occurred between the ages of 40 and 70 years.

In four of the five cases included in the mortality statistics the Andresen therapy was not strictly followed. One patient did not have an acute gastric hemorrhage, having had tarry stools for three weeks, and the diagnosis of bleeding ulcer was not definitely established. Another was exsanguinated on admission (red blood count 850,000; hemoglobin 10 per cent) and died within twenty-four hours. The third died after a massive transfusion not advocated here; the fourth was given 500 cc. of intravenous dextrose (also contra-

indicated) and died in sixteen hours. Thus the mortality rate in cases in which the regimen outlined was strictly followed is only 1.3 per cent.

When various mortality statistics are compared, variations of from 1 to 20 per cent are found, the rate being consistently higher whenever there was surgical intervention. At one hospital five out of seven patients who were operated on died; at another all died. It is indeed rare that an acutely bleeding patient recovers after a surgical procedure, and the operation, once performed, affords no guarantee of freedom from recurrent hemorrhage, for Balfour [5] found that 13 per cent of all patients had recurrent bleeding after operation. Hinton,[6] Westermann [7] and Hurst [8] also observed recurrent hemorrhage after surgery. Lynch [9] reported twenty-one cases surgically treated with a mortality of 42.8 per cent and thirty-one cases medically treated with a mortality of 12.9 per cent. Four of our patients had recurrent hemorrhage following gastric surgery.

TABLE 2.—*Long Island College Hospital Diet for Patients with Gastric Hemorrhage*

	Character of Feedings	Ounces	Grams	Calories
Gelatin solution	Gelatin	1	30	128.0
	Lactose	3	90	360.0
	Juice of 1 orange			
	Water	32	1,000	47.8
Gruel mixture 1	Cereal gruel (oatmeal, barley or cornmeal)	16	500	338.5
	Milk	14	420	290.8
	Cream	4	120	458.9
	Lactose	3	90	360.0
Gruel mixture 2	Cereal gruel (same)	12	350	227.5
	Milk	32	1,000	692.0
	Cream	4	120	458.9
	Lactose	4	120	480.0

Schedule of Feedings		Ounces	Total Calories
First and second day; feed every 1½ hours	Gelatin sol.	4	947.2
Third day; feed every 1½ hours	Gelatin sol.	4	
	Gruel 1	5	1,365.4
Fourth day; feed every 1½ hours	Gelatin sol.	5	
	Gruel 1	5	1,499.3
Fifth and sixth day; feed every 1½ hours	Gelatin sol.	6	
	Gruel 2*	6	3,600.0
Seventh and eighth day; feed every 2 hours	Gelatin sol.	6	
	Gruel 2*	6	3,600.0
Ninth day and thereafter	Long Island College Hospital diet for patients with ulcer		

* Add to gruel mixture at each feeding one of the following: 3 ounces of cereal, 1 soft poached egg, custard or jello.

It may be concluded that a certain percentage of patients with bleeding ulcer will die regardless of treatment, but the fundamentals of therapy must be met by aiding the physiologic processes of healing. This can best be done by putting the stomach as nearly at rest as possible, inactivating the gastric secretions and maintaining the general nutrition. The modified Lenhartz regimen of Andresen meets all these criteria physiologically and will, it is hoped, find a deservedly wider use in the future.

Minneapolis General Hospital.

5. Balfour, as quoted by Hurst.[8]
6. Hinton, J. W.: Hemorrhage in Peptic Ulcer, Ann. Surg. **101:** 856-862 (March) 1935.
7. Westermann, J. J.: Bleeding Gastric and Duodenal Ulcers, Ann. Surg. **101:** 1377 (June) 1935.
8. Hurst, A. F.: The Incidence, Mortality and Treatment of Hemorrhage in Gastric, Duodenal and Anastomatic Ulcer, Guy's Hosp. Rep. **86:** 135 (Jan.-April) 1936.
9. Lynch, R.: An Analysis of Ulcer of the Stomach and Duodenum, Canad. M. A. J. **17:** 677 (June) 1927.

ABSTRACT OF DISCUSSION

DR. ANDREW B. RIVERS, Rochester, Minn.: All are fairly well agreed that surgical rather than medical treatment is usually the procedure of choice in dealing with massive hemorrhage due to peptic ulcer. However, during or immediately after a hemorrhage the patient is either too sick or not sick enough to be operated on. To rush precipitously and tie off some bleeding vessel as a final gesture to save the life of the patient, it seems to me, is to court disaster. The time to operate on the patient who has bleeding peptic ulcer is in between the hemorrhages and before the final one has started. How shall one proceed when confronted with the necessity of doing something for the patient who has just had a massive gastric hemorrhage? Shall one begin at once on a regimen of feeding this patient? Shall one starve him until all signs of bleeding have stopped or shall one do a little watchful waiting for a few days while gradually restoring physiologic equilibrium, unless gross bleeding requires emergency transfusion? I have been depending mainly on the latter method, varying it somewhat to suit the individual case. The less severe the hemorrhage, the earlier I begin cautious, small, bland feedings. I am less timid about transfusion than is Dr. La Due. I agree with him that one of the important procedures in the treatment of such patients is to keep the stomach as completely at rest as possible. In addition, I should like also to keep the esophagus and the upper portion of the small bowel at rest. Frequently it is impossible to be certain before initiating treatment for gastric hemorrhage regarding the exact cause of such a symptom. Occasionally such an emergency is caused by bleeding esophageal varices. Under such a condition the institution of immediate and repeated feedings, particularly according to the Meulengracht method or after the passage of tubes for drip therapy, might well hinder rather than help the clotting of the blood. Furthermore, I have seen instances in which the restraining clot in a pancreaticoduodenal artery could scarcely have withstood any but the most innocuous gastric chyme impinged on it through a pyloric nozzle. If the gastric chyme can be made innocuous by the addition of gelatin mixtures this would constitute a sound physiologic reason for the use of gelatin after hemorrhages. I am not so convinced that any therapeutic procedure that requires frequent efforts of swallowing can prevent some peristaltic rushes in the upper portion of the gastrointestinal tract. These peristaltic rushes might defeat the purpose of frequent feeding.

DR. KENDALL A. ELSOM, Philadelphia: I agree with Dr. La Due that the treatment of bleeding peptic ulcer by a feeding program deserves a wide clinical trial. In an analysis of this problem last year Dr. Miller and I collected from the literature over 5,000 cases of peptic ulcer hemorrhage that had been treated medically by the usual conservative methods. The mortality was 9 per cent. In 509 similar cases in which food was permitted from the onset of bleeding the mortality was 1.8 per cent. If this striking reduction in mortality is achieved by future observers, a great advance in treatment will have been made. Dr. La Due's paper, since it bears on this point, is most timely. Let us examine whether or not he has demonstrated a reduction in mortality. One of the greatest difficulties in forming a definite conclusion concerning mortality rate is due to the fact that authors use different criteria for including or excluding cases in their statistical analyses. Let me use the data just presented as a case in point. Of the eight fatal cases one death was from pneumonia, not from loss of blood, and is properly excluded in calculating the mortality; one case was not treated with the Andresen diet and should, I think, be entirely excluded. The two in which death occurred before feeding could be instituted must be accepted as deaths from hemorrhage, for I doubt that Dr. La Due would contend that feedings of gelatin would have saved these patients in their moribund state. The two patients who died following transfusion and intravenous infusion can be excluded only if it is certain that these measures were directly responsible for their deaths. By a slightly different interpretation of the data, therefore, it is possible to arrive at a mortality figure of either 1.3 per cent or, according to my calculations, six deaths of eighty-one patients, or 7.4 per cent. If the latter figure is

correct it approximates the average 9 per cent mortality figure for the now current medical methods of treatment and does not establish an obvious superiority for the feeding technic. If the figure of 1.3 per cent is correct the feeding technic is clearly superior. On the basis of the data presented I feel that the lower mortality figure cannot be accepted. However, the main thesis of Dr. La Due's paper is entirely acceptable, and the wonder is that the technic introduced by Dr. Andresen in 1927 has not had wider acceptance in this country. Last year we adopted as a routine the essential elements of this regimen in the University of Pennsylvania Hospital and in ten cases have not yet had a mortality. Certainly the patients are in better physical and mental condition when fed regularly. We have followed the same general principles concerning transfusion that Dr. La Due outlined.

DR. HORACE W. SOPER, St. Louis: In 1931 my paper on the subject of "The Treatment of Hematemesis by the Retention Catheter" was published in THE JOURNAL. At that time I emphasized the use of the No. 16 gastroduodenal catheter in early lavage of the stomach. The catheter is introduced intranasally, contains no metal tip and is shaped like the ordinary urethral catheter, and the clots of massive hemorrhage can be washed out with a large Luer syringe perfectly, without any struggle or inconvenience to the patient. Furthermore, the tube can be easily passed in the unconscious patient. I advocated the early use of both gelatin water and egg albumin water and found that their use did not incite gastric secretion or gastric movements. Neither does the retention of this small catheter incite gastric secretion. About 25 to 50 per cent of the fluid that is put in the stomach passes out through the rubber tube. The remainder passes down into the small intestine. Distention of the stomach is thus prevented. Since that paper was published I have had increasing experience with the method and I feel that it has tremendous value, particularly in cases in which hemorrhage recurs. The physician is always in complete control of the situation. He knows whether or not any further bleeding has occurred. In the event of the recurrent or continued bleeding, one will see the blood coming into the glass tube that is attached to the container on the floor. One may now resort to early surgical treatment. Late surgery entails a high mortality percentage. Since 1931 I have encountered four cases in which early surgery was employed because of this appearance of the bright red blood after lavage, and all four patients recovered. In each instance the surgeon located the spurting artery.

DR. L. WALLACE FRANK, Louisville, Ky.: Dr. La Due has presented an interesting paper. Some of the most severe hemorrhages from the upper part of the gastrointestinal tract do not come from the ulcer itself but are due to erosions in hyperplastic stomach mucosa or the mucosa of the duodenum, and it is of these that I wish to speak. In a small series of cases in the past eight months the amount of blood loss in each varied from 500 up to 2,000 or 2,500 cc. No ulcer could be demonstrated. In this series in every case of hemorrhage the blood prothrombin as determined by the Quick method was 70 per cent of normal or less. These cases in which bleeding occurs from erosions are not surgical cases and the prothrombin level is below normal. The treatment consists in raising the blood prothrombin to normal and then the clot will be sufficiently strong to hold and the hemorrhage will cease. In this small series vitamin K was administered by mouth to raise the prothrombin, and drip transfusions of large amounts of blood were used to combat the blood loss. The transfusion is given relatively slowly and the blood must be taken from donors shortly before it is administered to the patient, as it has been demonstrated that blood kept in a "blood bank" loses its prothrombin value. Prothrombin in the donor's blood may cause temporary cessation of bleeding but to cure the patient it is necessary that his own blood prothrombin be raised to normal.

DR. WILLARD D. MAYER, Detroit: At the Receiving Hospital in Detroit we have used the Meulengracht method. We feed these patients. I must say that we started out with a considerable degree of fear, but our fears were really not justified. The Meulengracht routine consists briefly of a day of starvation at the onset of treatment with intravenous dextrose and transfusions as indicated, and then on the following day the patients are fed. We allowed the patients plenty of food; in fact, we gave them more than Meulengracht advised because we found that on his routine the patients had a considerable amount of food in the morning and at noon, but toward evening they were all very hungry so we increased the late afternoon and evening meals. Strange as it may seem, our results were pretty good. We had two deaths in a series of 113 cases. I really do not think one of these deaths should be considered as a death due to the diet, because one patient passed away within forty-eight hours and had but little to eat. The second case was a frank death incident to the diet. We had failures. Fourteen patients had to discontinue the diet because of abdominal pains or relapse of bleeding. These patients were taken off the diet. The treatment was not followed by me alone; it was followed by all members of the staff in the medical service as we wanted to get an unbiased opinion. Dr. La Due and some of the discussers have felt that in the empty stomach there is more vigorous peristalsis and more chance for hemorrhage. It seems to me that deaths in this condition occur either early at the onset or on the sixth or eighth day after the hemorrhage. I believe that with the feeding method those deaths occurring later are perhaps obviated. I would not say that this method is the last word; I think it should be carried on in other clinics and in this way it may be possible really to learn if the method is advisable. We did not have to give these patients large amounts of sedatives and opiates as they were comfortable after a few days, and their period of hospitalization was shortened. I believe there is merit to this routine.

DR. JOHN M. BLACKFORD, Seattle: I have recently reviewed the literature in an attempt to find out what the actual mortality is and have made a study of the subject in a new way. Dr. Cole and I went to the Seattle Bureau of Vital Statistics and took all the certificates of death from peptic ulcer for four years, 216 deaths. Seventy-two of the death certificates mentioned hemorrhage as a factor in death. We went back to the original hospital records of these seventy-two patients, or to their physicians, and found that fifty-five had actually died from hemorrhage. Four of these had died from hemorrhage from a gastrojejunal ulcer and hence should be excluded, leaving fifty-one patients who died from hemorrhage from peptic ulcer. Forty-nine of the fifty-one were above 45 years old, for only two deaths occurred in patients under 45 years of age. Forty-three per cent of the cases came to autopsy. In our experience we have had no deaths from hemorrhage in a patient under 45 years old. We have found, as has every other observer that I know of who has studied the matter in relation to age, that practically all deaths from hemorrhage (provided the surgeon lets the younger ones alone) occur in the older group. The mortality between 50 and 70, as found in various series of statistics, is about 30 per cent if only massive hemorrhages are considered. If all admissions for hemorrhage between these ages are considered, the mortality is approximately 15 per cent. The author has not discussed age groups at all in his paper, and I was a little disconcerted to find that his 1.2 per cent mortality was culled out of eight deaths in a series of eighty-two or eighty-three patients. The interpretation of statistics is always an interesting subject and it does not seem to me that we are justified in eliminating deaths because of some slight variation in treatment. I think it can be stated without any question that, from the practical standpoint, almost no deaths occur from bleeding from peptic ulcer in patients under 45 years of age. I think it impossible that there can be any radical error in our statistics. We are manifestly not using a sampling method when we have investigated all deaths in four years for a city of nearly half a million people. Such statistics are manifestly not based on a "sampling method." Regardless of what method of treatment is used in attempting to control hemorrhage from peptic ulcer, there are practically no deaths from such hemorrhage in patients under 50 years of age.

DR. MANFRED KRAEMER, Newark, N. J.: I want to make two points: First, there is no condition in internal medicine in which individualization is so important as in the treatment of bleeding peptic ulcer. Five years ago every patient who

came into the hospital was automatically put on starvation and then on a Sippy diet. Now every patient is given the so-called Swedish diet. Ulcer patients have to be individualized. An ulcer patient who is vomiting can't be fed. I have seen physicians following a printed routine go ahead and try to feed this Swedish diet to patients who are vomiting. There are many cases in which one has to give intravenous infusions, sometimes for several days. One has to treat the patient and one can't follow a feeding routine. The second point is the diminished importance of considering chemical neutralization of acid by feeding or by alkalis. The use of the gelatin may not be a neutralizing but an adsorptive mechanism. We should consider it thus more of a method of adsorbing (physical) acid rather than of neutralizing (chemical) acid. As time goes on we seem to be getting away from the thought of neutralization.

DR. WALTER L. PALMER, Chicago: I should like to point out that the Meulengracht diet, if it possesses any advantage over starvation, as it apparently does, probably does so by virtue of its ability to neutralize or absorb a certain amount of hydrochloric acid. A number of years ago Sippy advocated the prompt institution of feedings and the use of alkali in the treatment of hemorrhage. I have followed this program in the main for the last ten or twelve years. Because I have had some deaths and some recurrent hemorrhages, I have from time to time tried other methods. I cannot report today a series of cases treated by any one method. In 230 cases of massive hemorrhage the mortality rate has been a little over 3 per cent. Five deaths occurred from exsanguination. One man under 30 died in the fourth hemorrhage. Autopsy disclosed a bleeding artery. Most of the patients have died in their first hemorrhage rather than in recurring hemorrhages. I have concluded that patients should be fed at once if they are not vomiting. I use the old program of Sippy and continue it through the night. One must be careful about alkalosis. Contrary to the chemists, calcium carbonate may produce alkalosis. But if one uses it with magnesium oxide or other forms of magnesia the alkalosis can be partially combated by the addition of salt to the diet. The mechanism of this effect is obscure. I agree with Dr. Rivers and others about the importance and value of transfusions. I believe they should be used early. It is true that the more transfusions one must give, the poorer the prognosis, but I had occasional deaths from not giving transfusions. One recovery occurred after eight transfusions and several after five or six transfusions. I agree that drip feedings and drip methods should be avoided, if possible, because of occasional cases of hemorrhage from esophageal varices and also because with drip feedings there tends to be a dryness of the mouth, which I think contributed to two or three pneumonias complicating hemorrhage. One of these patients died from his pneumonia in spite of massive serum therapy.

DR. S. KENDIG WALLACE, Baltimore: I want to ask Dr. La Due why he didn't mention the use of larostidin in the treatment of peptic ulcer. I have been using it for several years in mild cases as well as in severe cases and with good results. In cases of severe gastric hemorrhage and of perforated peptic ulcer I start off immediately with two doses, that is 5 cc. twice a day, until the patient is out of danger. Regardless of what other treatment is used, I always use these injections as an additional precaution, which I feel is of considerable benefit to the patient.

DR. GORDON H. IRA, Jacksonville, Fla.: I listened to Dr. Andresen's paper in Washington in 1927 when he reported a series of cases in which this diet was used. For eleven years I have used it exclusively on service and private patients, with a very low mortality rate. One severe surgical critic, who treated all his patients with morphine and ice bags, has started using that diet. I want to commend Dr. Andresen's diet as Dr. La Due has reported it.

DR. JOHN S. LA DUE, Minneapolis: I hope to correct any false impression I may have given in discussing our mortality statistics. Some of the deaths occurred before any treatment could be given and are justly omitted in discussing the mortality of treated cases. Patients not receiving the exact treatment outlined here were included in gross mortality statistics. The figure 1.2 per cent was submitted only that you might know the death rate among patients given the exact regimen of therapy described here and I make no claim that these patients would have lived had this method been strictly followed. Larostidin was not employed in the treatment of our patients and hence we had no chance to appraise it. Dr. Soper's use of a catheter passed into the stomach or duodenum might be a valuable aid in determining which patients continue to bleed profusely and are therefore candidates for surgical intervention. The passage of such a tube and its continued presence near a bleeding ulcer are not without danger, I think. As yet we have no criteria to tell us which patients will die if treated by medical means alone, but surgical mortalities are far too high to make surgical intervention the method of choice except for the unusual case. I do not believe that we can say that the bleeding from peptic ulcer does not cause death. The complications of shock and the effects of prolonged loss of blood accounted for all but one of the deaths reported here. Deaths are not entirely confined to elderly patients; one of our fatalities occurred in a man 20 years of age.

HARD FACTS ABOUT PSYCHIATRY

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I can understand the dismay that must have filled the heart of the old-time medical practitioner when, shortly after the World War as the new dynamic psychiatry—then a lusty infant with new, esoteric phrases and glib terminology—when, as I say, he came face to face with the new psychiatry for the first time! How his head must have whirled as he had the newly developed professional jargon thrown at him by some enthusiastic protagonist of the "new psychiatry." Because it was the World War that brought the so-called "new psychiatry" into prominence.

A psychiatric conference in those postwar strongly freudian days was an interesting and an awesome thing; new phrases, new words, new ideas were coined by each new adherent to the school of dynamic psychiatry. Conservative members of the profession were nearly engulfed in a sea of complexes, fixations, transferences and cross transferences, and they swam hopelessly against being engulfed in a veritable deluge of metaphysical and highly theoretical hypotheses.

So strong was this school of thought that it could not be held within the bounds of the medical profession but seeped over, adding salt—and perhaps a bit of salaciousness—to the drama, the arts, literature and even into the drawing room, where buxom ladies, bosoms billowing over tea cups, with a slightly self-conscious air, discussed the goings-on of their libido, their father fixation—"Electra" complex to you—and used words, which, in their more innocent days they would have thought obscene.

The dramatist O'Neil seized on it, and we learned of some of the strange, morbid undercurrents of the mind, through his Strange Interlude, Mourning Becomes Electra, and other productions. Lesser dramatists sensed the fact that there was gold "in them thar hills" and worked a rich tapestry of phallic symbolism into their work. Soon it was difficult to see anything but plays in which maladjusted individuals killed each other off in response to hidden urges or complexes having their roots in the dim, atavistic past, while novelists plied busy pens exposing, from another point of view, the miserable and degrading thoughts of men.

Read before the Section on Preventive and Industrial Medicine and Public Health at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 19, 1939.

In short, for a period America was extremely self conscious, introverted, and the well informed freudian was fearful of even the slightest little mannerism, lest he betray to his colleagues the fact that he was still a polymorphous pervert.

Those were happy days for some of the profession. It was before the depression and there were any quantity of neurotic, self-centered ladies and gentlemen who were willing to pay for the privilege of having the opportunity of talking about themselves and the state of their feelings in a dimly lighted room and to a sympathetic gentleman just lately returned from Vienna!

Small wonder that the general practitioner, the ophthalmologist, the pediatrician and the internist looked slightly aghast and made a mental note in confirmation of their previous estimate of psychiatrists and psychiatry.

But enough: I would not have you believe that I am belittling Freud or the remarkable contribution he has made to present day psychiatry. Rather, I have tried sketchily to point out the strange exotic atmosphere which prevailed in this country when Freud's teachings burst upon the public. Before Freud, psychiatry was static, hopeless and sterile. He breathed new life into it, and he gave us as we never had before an understanding of the human mind as a complex and dynamic thing. He destroyed in one brief year the artificial and highly dynamic structure of kraepelian definitive psychiatry, which was so concerned with disease labels that it did little about the disease itself.

But, much as we gained from Freud, there were losses too for a time. There was a loss because the ascendancy of the psyche over the soma resulted in an almost exclusive study of mental illness so called, from the psychogenic angle, and with consequent slowing up of other approaches.

There was a tremendous upswelling of interest in Freud's wake and with the usual results: the opportunist, the zealot, the quack and the scatterbrained seized on it—for sincere purposes in some instances, for exploitation in others. The more enthusiastic hailed it as a panacea for all human ills—the criminal was going to be reformed, the behavior problem was going to be eliminated, the psychotic was going to be restored to sanity. There was no claim too far reaching, too extravagant, and as a result the public was led to expect miracles.

Gradually, members of the medical profession began to look with even more skepticism than usual on this strange, scarcely acknowledged child of the medical family. They could not understand why some of its members, working in the name of science, should be so wholly lacking in scientific objectivity—so obviously moved by emotion rather than by reason. Psychiatry was then under the bar sinister in the family of medicine, and those who were in psychiatry, who weren't entirely satisfied to have the psyche run away with the soma, could do little but tend to their knitting.

And this modest tending to business, letting others save the world, this tending to knitting has begun to produce results, such results as make it possible for us to state here today that psychiatry does now take full account of both somatic and psychic disorders and that the real psychiatrist is aware more than ever before of the interdependence of the mind and the body. He realized that a sick body can make a sick mind or, conversely, that a sick mind can make a sick body.

Most physicians are aware of the signal advances made since the turn of the century in the field of psychiatry. First there was Wagner von Jauregg's discovery of malarial therapy for dementia paralytica. Previously a variety of so-called disease entities, carefully labeled, were attributed to psychogenic causes; when malarial therapy was applied, however, it was discovered that the spirochete had various ways of manifesting its presence, depending on the type of personality of the sufferer and his constitutional predisposition, so that at one fell swoop a dozen different so-called mental diseases had a segment sliced off them.

It was a severe blow to the exclusively psychogenic school of thought!

We are aware of the mental symptoms associated with pellagra—and now we know that nicotinic acid will clear up these symptoms miraculously. We are aware of the symptomatology associated with an alcoholic psychosis which is really chronic poisoning, and the nutritional deficiencies manifest in neuritic disorders, now markedly influenced by vitamin therapy.

But the end was not there: workers in the field of electro-encephalography were adding still further proof to the rapidly accumulating evidence of the body's influence on the mind.

Gibbs, Davis, Lennox and other workers in the field of brain waves were building up a new conception of the human brain as a pulsing, dynamic thing, with a rhythm as constant and observable as the systole and diastole.

For the first time in medical history it was possible to record constitutional activities of the brain itself with as much clarity and accuracy as an electrocardiograph. Through the charting of these brain waves they discovered that the brain itself suffers from a dysrhythmia, a momentary spasm, in certain nervous disorders such as epilepsy, and that these dysfunctions could be recorded. For example, the rhythm was completely destroyed during an epileptic seizure. Psychogenic? Perhaps.

Within the past month Lennox and Gibbs have announced that carbon dioxide will influence the brain rhythm. If an epileptic patient pumps carbon dioxide from his lungs and blood by breathing hard, a seizure may result, and conversely, while he is breathing air which contains an increased concentration of carbon dioxide, petit mal ceases. It has been demonstrated that the electrical pattern of the brain is extremely sensitive to small changes in the carbon dioxide of the blood passing through it. Furthermore, there is every reason to believe that not only epilepsy but other forms of mental disorder may also be caused by a condition which produces a form of dysrhythm in the brain.

This relationship must, of course, be carefully worked out, but it would seem that here too the laboratory technician, the chemist and the careful physician who is basing his experiments on the foundation of good physical medicine are well on their way to making another valuable contribution.

There is reason to believe too that this line of experimentation is not too far removed from insulin and other shock therapy which produce anoxia or temporary nutritional deficiency in the brain, producing shock, which in turn has been found to be quite efficient in producing remissions in severe cases of mental disorder. There are some, of course, who state that the results of shock therapy are partly "psychological." But they do actually produce brain changes. What their precise mechanics is we are not yet prepared to

say, but their use as a therapy for the more severe psychoses has added still another weapon for the psychiatrist.

In this brief paper I can do little more than give a hint of some of the developments in psychiatry which are proceeding on good, solid ground. Important work is also being done in the field of endocrinology and allergy, and many are convinced that some forms of mental disorder can be traced to these sources.

But out of the entire field of developments emerges one significant fact, and that is psychiatry has come of age and is now working objectively, scientifically and with medical weapons to combat the biggest health problem in the country.

Even in psychotherapy there has been a radical revision of thought. Education and reeducation have become the keystone in all progressive hospitals, even though some may call it by other fancier names, and purposeful, constructive work of therapeutic value is being substituted for the old fashioned occupational therapy of yesterday. The patient now has a chance to leave the hospital possessed of training and with his field of interest broadened, his capacities for the enjoyment of life enlarged and his whole personality enriched by the training that has been given him.

But while considering these factors one must not lose sight of the other angle—that while the metaphysician and the psychogenist stand at one end of the axis, at the other end stands the stodgy organicist who believes nothing that he can't see under a microscope or that can't be extirpated with the surgeon's knife. No one will ever know how many neuroses have survived the removal of healthy gallbladders, removed by too materially minded surgeons, or how many appendixes have been removed, how many stomach ulcers treated, with no thought of the possibility of psychogenic background.

The work of Cannon in demonstrating psychosomatic relationships and the more recent work of Dunbar and others in showing the interrelationship of psyche and soma in many disease conditions must necessarily revise the old fashioned conception of disease as merely "disease tissue" and force a return to an earlier conception of the patient as a whole and not a collection of bone and various other tissue. We must be constantly aware that a stomach ulcer can be the end result of a psychic disturbance, just as we must realize that a psychic disturbance can be the result of a physical dysfunction or nutritional deficiency.

Happily the two ends of the axis are coming together. Soon, we hope, there will be no such thing as a psychogenic school and an organic school. The practicing physician will realize the importance of psychogenic factors and the psychiatrist will know the possible contribution of the various dysfunctions to a mental condition.

In fact, I think the day is coming when we shall stop talking about "mental disease" and "physical disease" because I am convinced it is an artificial and wrongful separation. The human organism becomes ill, and one cannot separate the human organism into separate entities any more than one can consider it apart from its environment. I say the distinction is an artificial one because it was thought that dementia paralytica was a "mental disease" and then was discovered to be caused by the spirochete. Does it now become a physical disease with mental symptoms? It may be demonstrated that there is scarcely a physical disorder that doesn't have its mental concomitants—a carbuncle on a patient's neck has a definite influence on his personality! More difficult, perhaps, but just as logical is the assumption that there is no so-called mental disease that does not have its physical concomitants which may ultimately be demonstrated.

And when that artificial distinction between mental disease and physical disease is abolished in the minds of physicians generally it will be a good thing for psychiatry and it will be a good thing for the internist. Psychiatry can well profit by the painstaking laboratory research of physical medicine, and physical medicine can in turn ingest psychiatry with its leavening interpersonal relationship and its awareness of the psychogenic factors which are present in practically all disease conditions.

The modern psychiatrist should be on friendly terms with a stethoscope and at all times be a doctor. The men in other branches of medicine learn to know and use "psychological medicine."

Meanwhile, it would be well for general practitioners to realize that psychiatry has come out of its swaddling clothes and that it now stands mature, young to be sure, but with its wild oats behind, ready to assist by certain definite contributions to the art and the science of healing.

ABSTRACT OF DISCUSSION

DR. W. A. SAWYER, Rochester, N. Y.: I feel that we are coming to a period perhaps when not only industry but also public health and other spheres of preventive medicine are going to have to think about this subject of psychiatry in more general and practical terms. Psychiatry has been tried in industry in a number of places and, if it has failed, it has failed I think because the emphasis has been put too much on the matter of the specialty rather than on the principles involved and making them applicable to the practical, everyday medical work. The point that I tried to emphasize in my paper last week was the thought that you could infiltrate into an organization, even into the employment of individuals and personnel problems, the best psychiatric principles and you could accomplish a great deal in the adjusting of individuals to their jobs and helping them to understand the problems which confront them in their daily work. We are fortunate to have had as practical a paper as Dr. Burlingame has given us this morning.

DR. JOHN A. FERRELL, New York: May I ask Dr. Burlingame what those of us in public health work, interested from the community standpoint and also from the preventive standpoint, are keenly interested to know? What can be done in addition to the development of local health organizations that will make possible the finding of these cases in childhood that represent departures from the normal, and what might be done in the community within ordinary economic regions and the expansion of the health department to head these cases off if possible before they reach the institutional stage? What would you do in the matter of national and state public health nurses serving the community? Many of us admit we know nothing about it, and we don't know how to get at it.

DR. C. C. BURLINGAME, Hartford, Conn.: I am very glad to answer that question. I don't think the preventive work of psychiatry will ever be done exclusively by psychiatrists. I think a large part of it will have to be done by men in other branches of medicine and I further believe that much of the educational work that must be done to prevent the increase in mental and nervous diseases is going to be done through departments of health. There is frequently a strange isolation between the mental hospital and the departments of mental hygiene on the one hand and the public and the general practitioner on the other hand. It is unfortunate that some departments of mental hygiene are so remote from the men who are practicing medicine. I have come to the conclusion that there is no more reason for separating the preventive work in psychiatry than there is for separating the work being done in preventing contagious diseases. I think they should go under the same general leadership, and in that way we shall get at the rank and file

of men practicing medicine. Usually, now when a patient gets to the psychiatrist the situation is pretty well developed. I am opposed to the development of great, powerful departments of psychiatry in state organizations or in medical schools, if such development prevents the free infiltration of psychiatric principles into all other branches of medicine. In fact, I am opposed to anything which would tend to isolate psychiatry from the general practice of medicine. As to how to prevent mental disease, that is what you gentlemen will have to tell us. We have talked about preventing mental disease for many years but we are still building bigger and better state hospitals and the only change that has really taken place in some of them is that their name has been changed from "asylum" to "hospital." I should like to see the intellectual walls of the state hospital torn down. I should like to see the doors open. And if you send your patient to the state hospital I see no reason why you shouldn't follow his progress in the hospital. In fact, if you will not come to the hospital of your own volition, I think you should be dragged there. You, the members of other branches of medicine, can do a great deal toward breaking up these isolated systems that now sometimes exist within our state hospitals. I think the first step is a closer rapport between the state hospitals and the general practitioner, through the destruction of the state hospital's all too frequent isolation.

CLINICAL AND EXPERIMENTAL STUDIES ON VITAMIN K

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It is our purpose in the present paper to discuss the bleeding tendency so often seen in patients having biliary fistulas or obstructive jaundice. In many of these patients death occurs from persistent hemorrhage. This hemorrhage may begin independently of known trauma, but usually it begins at operation or appears from the wound after operation. It is now known that the bleeding is due to abnormal lowering of the plasma prothrombin level and that in most cases the bleeding tendency can be relieved by vitamin K therapy. We wish to outline the experimental and clinical work on which this theory is based, and along with this we wish to describe, briefly, a simple method that we [1] have recently devised for the recognition of the vitamin deficiency. With the aid of this test it is now possible to obtain information at the bedside regarding vitamin K requirements. It is also a simple matter to determine, from time to time, the effect obtained from vitamin K already given.

HISTORICAL SKETCH

The existence of vitamin K was first suspected from experiments done nine years ago by Dam [2] of Copenhagen. In some studies on lipoid metabolism, newly hatched chicks were placed on a fat-free diet. After several weeks these chicks developed hemorrhages into the skin, mucous membranes and other portions of the body. This work prompted further study, and it was demonstrated that a new fat-soluble vitamin is essential for the prevention of this bleeding tendency. The Danish word for "coagulation" resembles the German word and is spelled "koagulation." The vitamin was therefore spoken of as "vitamin K."

Subsequent studies by Dam and his colleagues [3] and by others,[4] notably by Almquist of California, showed that: (*a*) Vitamin K is present in large amounts in certain green vegetables such as alfalfa, spinach and kale. The vitamin is a colorless compound, however. (*b*) The vitamin can be produced by bacterial action and is therefore present in the lower portion of the intestine, even when the animal is maintained on a diet free of the vitamin. Absorption from the lower part of the intestine is minimal in the chick, but in mammals absorption does occur and hence mammals rarely show vitamin K deficiency [5] except in cases of faulty absorption. (*c*) By rather elaborate chemical technic it has been possible to isolate the vitamin in the form of a highly potent oil. The chemical composition of the oil is not known, and reports [6] indicate success in obtaining this compound in crystalline form. (*d*) In chicks maintained on a diet free of vitamin K it was found that the prothrombin level was low, and this explained the bleeding. It has not yet been determined whether vitamin K enters chemically into the formation of prothrombin or whether the vitamin merely keeps certain tissues in a normal healthy state of activity essential for the formation of prothrombin.

As has been stated, mammals, including man, obtain vitamin K both from the diet and from bacterial activity in the intestine. A vitamin K deficiency develops when absorption of this particular compound from the intestine is interrupted. Faulty absorption occurs when bile is excluded from the intestine. Bile has long been known to aid in the absorption of fats. Vitamin K is a compound having the solubility properties of fats, and without bile or bile salt it cannot be absorbed. In obstructive jaundice or in patients with biliary fistulas the intestine receives no bile and hence the absorption of vitamin K is interrupted. After a few weeks or months the plasma prothrombin level falls and a tendency to bleed develops.

Treatment consists in feeding bile or bile salt, along with large amounts of vitamin K, to supplement the natural supply. This use of vitamin K in obstructive jaundice was first proposed on theoretical grounds by Quick,[7] though he made no direct tests to prove the

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validity of his proposal. In fact, in one case, which he[8] reported later, a patient on vitamin K therapy failed for some reason to respond.

Historically, the first direct evidence reported in support of the new theory was supplied by Greaves and Schmidt.[9] They showed that in rats with biliary fistulas a prothrombin deficiency develops, thus confirming similar observations of Quick, Stanley-Brown and Bancroft[10] made in human cases of obstructive jaundice, and of Hawkins and Brinkhous[11] in dogs with biliary fistulas. They also found that this deficiency could be relieved by feeding vitamin K and bile salt. Two months later the first successful treatment of human patients was reported from our own laboratory,[12] and our report was followed immediately by a report of similar results obtained by Butt, Snell and Osterberg[13] at the Mayo Clinic. Since that time confirmatory evidence has been supplied by Dam and Glavind,[14] our laboratory,[15] the workers at the Mayo Clinic,[16] Olson,[17] Stewart[18] and Rhoades.[19]

Recent work from this laboratory[20] has shown that the liver is concerned in the manufacture of prothrombin. When the liver is partially excised or is injured by poisons, infection or tumor growth, the level of plasma prothrombin falls. In these cases there is no vitamin deficiency, and feeding vitamin K does not cure the condition.

DETECTION OF VITAMIN K DEFICIENCY

Vitamin K deficiency is to be suspected in all cases in which there are biliary fistulas or obstructive jaundice. The degree of deficiency tends to be greatest in cases of long duration but is sometimes marked when obstruction is of recent origin (from two to three weeks). If a deficiency does exist, it is important that the patient receive vitamin K therapy for several days before any operative procedures are undertaken. Any attempt to treat all suspected cases as a routine will result in needless delay in those cases in which vitamin K deficiency is not yet present. The ordinary tests for bleeding and clotting time reveal the abnormality only when the prothrombin deficiency is extreme. They give normal values when the plasma prothrombin level is merely approaching the danger zone. These tests, therefore, fail when they are most badly needed. The two stage technic for the titration of prothrombin developed in this laboratory[21] gives the most exact measure of the vitamin deficiency yet devised, and for purposes of research this technic is to be recommended. However, the method is too complex for routine clinical use. The one stage method of Quick[22] is less specific as a test for prothrombin but it is simpler from a technical standpoint. Even so, it requires the collection of blood in oxalate, the use of the centrifuge and finally a titration procedure. A test which we have recently devised[1] is similar in principle to the test of Quick but is carried out on whole blood at the bedside and is so simple that it can be mastered with very little practice.

A New Test for Vitamin K Deficiency.—With a serologic pipet, 0.1 cc. of thromboplastin, described in the next paragraph, is placed in a small serologic tube (75 by 10 mm. outside diameter). In the tube is then placed blood, freshly drawn from the patient, up to a 1 cc. mark previously made on the side of the tube. The tube is at once inverted over the finger to obtain complete mixing of the blood and thromboplastin. The tube is tilted every second or two in order to observe clotting. As a control, the test is also carried out on the blood of a normal subject. The calculation is as follows:

$$\frac{\text{Clotting activity}}{\text{(in percentage of normal)}} = \frac{\text{Clotting time of normal control}}{\text{Clotting time of patient's blood}} \times 100$$

Thus, if the patient's blood clotted in forty-eight seconds and the normal person's blood in twenty-four seconds, the clotting activity is calculated to be 50 per cent of normal.[22a]

To prepare thromboplastin, fresh lung of ox or rabbit is ground, and to each 10 Gm. portion is added 10 cc. of physiologic solution (0.9 per cent) of sodium chloride. This is stirred at intervals for several hours. The fluid then obtained by straining through gauze is the "thromboplastin" employed in the test described. This thromboplastin keeps well in the ice box.

Interpretation of Results Obtained with the Test.—The new test is not as specific for prothrombin as the two stage method[21] that we use for purposes of exact research. However, the new test, like that of Quick,[22] is a presumptive measure of the amount of prothrombin present in the plasma. Work from this laboratory[23] has shown that other factors do influence the reading. Thus, in some cases the prothrombin is more easily converted than in others, and this compensates for a deficiency in the amount of prothrombin. The new test, like that of Quick, measures a summation of the amount of prothrombin and of its "convertibility." One thus obtains a very practical measure of the tendency to bleed. Experience with a large group of

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21. Warner, Brinkhous and Smith.[20] Smith, Warner and Brinkhouse.[20]

22. Quick, A. J.: On Various Properties of Thromboplastin (Aqueous Tissue Extracts), Am. J. Physiol. **114:** 282 (Jan.) 1936.

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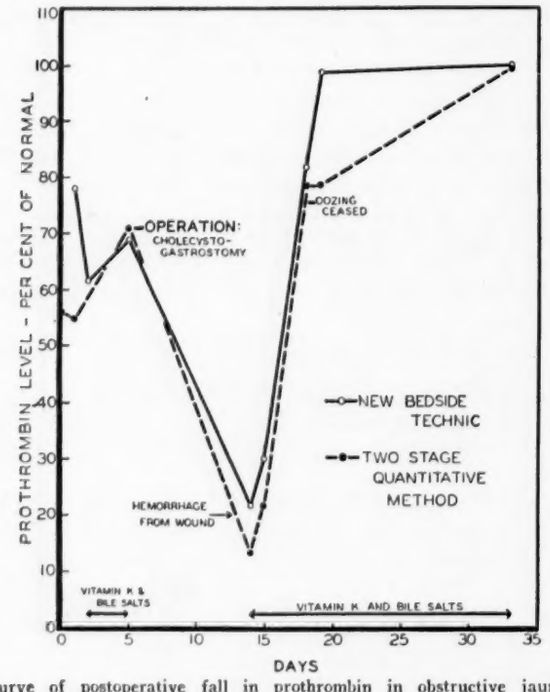
patients having biliary fistulas or obstructive jaundice shows that bleeding commonly occurs when the test gives values of 40 per cent or less. In extreme cases, the level falls as low as 15 per cent of normal. Values of from 40 to 70 per cent are definitely in the danger zone.

THERAPEUTIC USE OF VITAMIN K

Vitamin K is readily obtained in crude form by the extraction of alfalfa meal with high-test gasoline (free of lead). The gasoline is removed by distillation, and the crude vitamin is emulsified in bile or in a 2 per cent solution of bile salt. The vitamin can be purified by a variety of chemical procedures, and recently a number of drug firms have undertaken to prepare the vitamin in a form suitable for clinical use. One of these preparations,[24] in capsule form and dissolved in oil, is already on the market. Another,[25] a cereal grass preparation, is supplied in powdered form. Preliminary work indicates that under certain conditions the vitamin keeps



Curve of postoperative fall in prothrombin in obstructive jaundice. Rapid recovery following administration of vitamin K and bile salts. Note close correspondence between prothrombin by old (two stage) method and by the new simplified test.

well at room temperature, but evidence [26] indicates that this is not true under all conditions.

Much is still to be learned about the amount of vitamin K to be administered. Some vitamin K is formed by intestinal bacteria and some is present normally in the diet; hence the daily feeding of bile prevents the fall in prothrombin incident to biliary fistula.[11] Feeding bile also restores the prothrombin level to normal in cases in which it has already fallen to low levels.[27] However, the recovery in such cases is slow unless the diet is artificially enriched with the vitamin. To obtain a rapid rise in the prothrombin level we make it a practice to administer daily the vitamin K extracted from 300-400 Gm. of alfalfa meal. Vitamin K assay technic is not well enough standardized to permit accurate comparison of the various products used in different clinics. Evidence now at hand indicates, however, that the dosage we employ is much larger than that used by certain other workers in this field and is possibly smaller than that used in some clinics. It is very important that methods of vitamin K assay be improved and standardized and the keeping qualities of the vitamin be carefully determined and controlled. When this is done the question of clinical dosage will be more easily studied.

In treating patients bile or bile salt must be fed along with the vitamin to aid in the absorption of the latter from the intestine. It is customary to feed daily at least an ounce of bile or its equivalent in the form of dried bile or bile salt. We have recently had two cases which failed to respond on this dosage when given along with the usual dose of vitamin K. They did respond, however, when the dose of bile was increased five fold, the dose of vitamin K being unchanged. It is probable that some patients require more bile than others; also that some require more vitamin K than others. Evidence now available indicates that bile salt may be as effective as whole bile, but further work is needed in regard to this.

The rate at which the plasma prothrombin level rises with vitamin K therapy varies in different cases. As a rule a definite rise occurs in twenty-four hours, but from three to eight days of treatment is usually needed to obtain the maximal response.

It cannot be emphasized too strongly that the vitamin treatment should be continued during the postoperative period,[28] especially if bile continues to drain from the wound. In addition to the lack of vitamin, such patients no doubt consume prothrombin in large amounts in forming fibrinous exudate in the margins of the wound. In all cases the clotting test, already described, should be performed every few days during the postoperative period in order to guard against a disastrous fall in prothrombin.

Finally, it need hardly be mentioned that vitamin K is of no value in the treatment of hemophilia or thrombocytopenic purpura. In these diseases there is no deficiency in vitamin K and no deficiency in prothrombin. Nor can one expect a response to the low prothrombin levels often present in cirrhosis of the liver or in cases of severe hepatitis. In these cases the "factory" that forms prothrombin is disordered, and the disease is not essentially one of vitamin K deficiency.

AN ILLUSTRATIVE CASE OF VITAMIN K DEFICIENCY

A white man aged 70 entered the hospital with the complaint of painless jaundice of two months' duration. The stools were clay colored and the urine was a dark yellow. Intense pruritus was present, and the patient had lost 10 pounds (4.5 Kg.). The gallbladder could be felt on palpation. Operation, performed by Dr. F. J. Jarvis, showed inoperable carcinoma of the ampulla of Vater. A stone was removed from the gallbladder. Cholecystogastrostomy was performed and the wound was closed without drainage.

Prior to operation the bedside clotting test on two occasions gave values of 78 and 62 per cent of normal. This was not considered in the danger zone, and vitamin K (from 300 Gm. alfalfa) and bile salt (30 cc. of 2 per cent solution) were given for two days only, without any well marked effect. (It has been our experience that patients in this zone are less likely to respond promptly than when the prothrombin lowering is more pronounced.)

Vitamin K therapy was discontinued following operation, and on the sixth postoperative day blood began to ooze in large

24. Abbott Laboratories, North Chicago, Ill. "Klotogen."
25. Cerophyl Laboratories, Kansas City, Mo. "Cerophyl."
26. MacCorquodale, D. W.; Binkley, S. B.; McKee, R. W.; Thayer, S. A., and Doisy, E. A.: Inactivation of Vitamin K by Light, Proc. Soc. Exper. Biol. & Med. **40**: 482 (March) 1939.
27. Greaves and Schmidt.[9] Warner, Brinkhous and Smith.[12] Butt, Snell and Osterberg.[12]
28. Scanlon, G. H.; Brinkhous, K. M.; Warner, E. D.; Smith, H. P., and Flynn, J. E.: Plasma Prothrombin and the Bleeding Tendency, with Special Reference to Jaundiced Patients and Vitamin K Therapy, J. A. M. A. **112**: 1898 (May 13) 1939. Stewart.[16] Footnote 16.

amounts from the wound. The bedside clotting test was 22 per cent of normal. Vitamin K and bile salt therapy was resumed and within two days the bleeding ceased and within five days the level had risen to 95 per cent of normal.

In this same case prothrombin determinations were also made by our two stage method, which is more specific for prothrombin. The excellent correlation with the bedside test is shown in the accompanying chart. For practical routine clinical use we are confident that the new test fulfils all essential requirements.

NOTE.—Since this paper was written, Almquist and Klose [29] have shown in chicks that phthiocol, a yellow compound prepared synthetically by R. J. Anderson, has vitamin K activity. Immediately thereafter work from that and other laboratories [30] showed that vitamin K activity was possessed by a number of other naphthoquinones.

With the aid of Dr. Joseph E. Flynn we have recently had success in the use of phthiocol intravenously in cases of obstructive jaundice. In one case, 45 cc. of 0.2 per cent solution in isotonic phosphate buffer (p_H 7.4), given in divided doses, raised the prothrombin from the 39 to the 75 per cent level in twenty-four hours. No toxic effect was observed. We are indebted to Dr. Anderson for the phthiocol used.

THE PREOPERATIVE AND POSTOPERATIVE ADMINISTRATION OF VITAMIN K

TO PATIENTS HAVING JAUNDICE

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Studies on the factors concerned in the production of hemorrhagic diathesis characterizing patients who have jaundice have been discussed in previous papers.[1] Numerous other investigators have demonstrated definitely that cholemic bleeding is caused by a deficiency of prothrombin in the circulating blood and that both this deficiency and the hemorrhagic state associated with it can be corrected by the administration of concentrates containing the fat-soluble antihemorrhagic vitamin K, together with bile salts to insure absorption of the vitamin. The early clinical application of this knowledge concerning vitamin K was begun independently in the United States by Warner and his associates [2] at the University of Iowa and by us, and abroad by Dam and his co-worker [3] in Copenhagen.

During the past two years we have continued our observations on this problem, several lines of investigation having been pursued. We have endeavored to determine the reliability of vitamin K concentrates in the control of bleeding of jaundiced patients and also to establish standardized methods of the preoperative and postoperative treatment of such patients. An investigation of the causes of failure among occasional patients who do not respond to the administration of vitamin K by an increase in the prothrombin content of blood and control of the hemorrhagic state also has been carried out. Finally, we have attempted to study other causes for a deficiency in the content of prothrombin, a matter which is concerned chiefly with defects in the absorption of this material. These studies constitute the basis of the present report.

THE CLINICAL PROBLEM OF CHOLEMIC BLEEDING

The earliest reported case of fatal bleeding in a patient having jaundice was made by Wedelius [4] in 1683. Since the advent of listerian surgical technic, the tendency to bleed which is peculiar to patients having jaundice has been a factor of grave concern to the surgeon. In the early reports by Musser and Keen,[5] Depage,[6] Greig Smith [7] and Mayo Robson,[8] hemorrhage accounted for a large part of the high mortality that accompanied the surgical treatment of the jaundiced patient. Even current figures indicate that cholemic bleeding has accounted for about 50 per cent of the mortality accompanying surgical intervention on patients having jaundice and that cholemic bleeding, of itself, imposes a surgical risk of approximately 5 per cent.

There is now general agreement that hemorrhagic diathesis in the presence of jaundice is not the result of any alteration in the amounts present of calcium, bilirubin, platelets, fibrinogen or thromboplastin. The original suggestion of Quick and his co-workers [9] that the condition depended on a lack of the one substance necessary for coagulation not previously studied, namely prothrombin, has now been amply confirmed. Evidence has also accumulated to prove that a particular fat-soluble material (that is, vitamin K) normally present in the intestinal tract, is absorbed and utlized by the liver in some unknown manner to maintain a normal concentration of prothrombin in the blood plasma.

The composition of prothrombin is unknown; it may well be defined, as suggested by Patek and Taylor,[10] as a physiologic complex known only by its capacity to form thrombin. For this reason, any method for measuring the content of prothrombin in the circulating blood must be considered an indirect one.

Concerning the mechanism by means of which vitamin K affects prothrombin we have no data and, until vitamin K is isolated in pure form, this phase of its physiologic activity probably will remain unanswered.

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29. Almquist, H. J., and Klose, A. A.: J. Am. Chem. Soc. **61:** 1611 (June) 1939.

30. J. Am. Chem. Soc. **61:** 1923-1932 (July) 1939.

From the Division of Medicine (Drs. Butt and Snell) and the Division of Biochemistry (Dr. Osterberg), the Mayo Clinic.

Owing to lack of space this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the authors' reprints.

Read before the joint meeting of the Section on Practice of Medicine and the Section on Pharmacology and Therapeutics at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 19, 1939.

1. (*a*) Butt, H. R.; Snell, A. M., and Osterberg, A. E.: The Use of Vitamin K and Bile in Treatment of the Hemorrhagic Diathesis in Cases of Jaundice, Proc. Staff Meet., Mayo Clin. **13:** 74-80 (Feb. 2) 1938; (*b*) Further Observations on the Use of Vitamin K in the Prevention and Control of the Hemorrhagic Diathesis in Cases of Jaundice, ibid. **13:** 753-764 (Nov. 30) 1938; (*c*) Snell, A. M.; Butt, H. R., and Osterberg, A. E.: Treatment of the Hemorrhagic Tendency in Jaundice, with Special Reference to Vitamin K, Am. J. Digest. Dis. **5:** 590-596 (Nov.) 1938.

2. Warner, E. D.; Brinkhous, K. M., and Smith, H. P.: Bleeding Tendency of Obstructive Jaundice: Prothrombin Deficiency and Dietary Factors, Proc. Soc. Exper. Biol. & Med. **37:** 628-630 (Jan.) 1938.

3. Dam, Henrik, and Glavind, Johannes: Vitamin K in Human Pathology, Lancet **1:** 720-721 (March 26) 1938.

4. Wedelius, D. G. W.: De haemorrhagia universali, ex ictero nigro lethali. Miscellanea curiosa medico-physica Academiae Caesarea Leopoldino-Carolinae naturalrum curiosorum, Lipsiae, 1670-1705; **2:** 318-319, 1683.

5. Musser, J. H., and Keen, W. W.: Cholecystotomy: With a Report of Two New Cases, a Table of All the Hitherto Reported Cases, and Remarks, Am. J. M. Sc. **88:** 333-367 (Oct.) 1884.

6. Depage, A.: Statistics of Operations on the Gallbladder, Lancet **1:** 89 (Jan. 12) 1889.

7. Smith, J. Greig: Abdominal Surgery, ed. 4, Philadelphia, P. Blakiston's Son & Co., 1891, p. 610.

8. Robson, A. W. Mayo: Diseases of the Gall-Bladder and Bile-Ducts, Including Gall-Stones, ed. 3, New York, William Wood & Co., 1904, pp. 264-268.

9. Quick, A. J.; Stanley-Brown, Margaret, and Bancroft, F. W.: A Study of the Coagulation Defect in Hemophilia and in Jaundice, Am. J. M. Sc. **190:** 501-511 (Oct.) 1935.

10. Patek, A. J., Jr., and Taylor, F. H. L.: Hemophilia: II. Some Properties of a Substance Obtained from Normal Human Plasma Effective in Accelerating the Coagulation of Hemophilic Blood, J. Clin. Investigation **16:** 113-124 (Jan.) 1937.

The recent report by Almquist and Klose [11] offers hope that pure vitamin K will soon be available.

For routine determinations of the content of prothrombin we have used the method of determining the prothrombin coagulation time as developed by Quick and his associates [9] and have found it well adapted for general laboratory use. In many instances we have also employed the quantitative method of study of blood

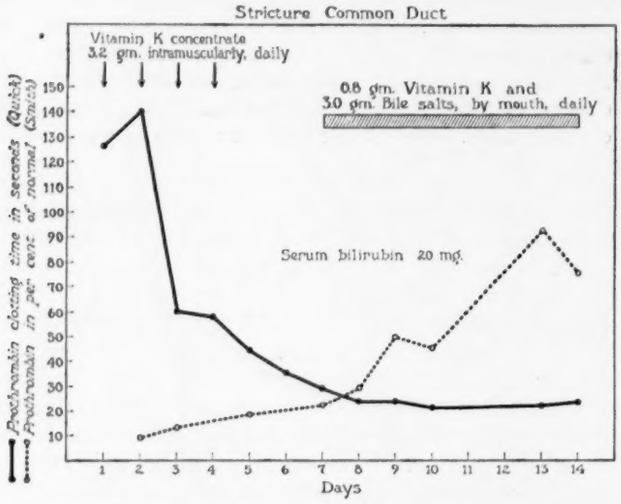
Stricture Common Duct
Vitamin K concentrate
3.2 gm. intramuscularly, daily
0.6 gm. Vitamin K and
3.0 gm. Bile salts, by mouth, daily
Serum bilirubin 20 mg.
Prothrombin clotting time in seconds (Quick)
Prothrombin in per cent of normal (Smith)
Days

Chart 1.—The effects of the parenteral administration of vitamin K concentrates on the prothrombin clotting time and the quantitative content of prothrombin in plasma, of a patient having stricture of the common bile duct.

clotting of Warner and his associates.[2] When "prothrombin time" or "prothrombin clotting time" is used subsequently it refers to the clotting time of recalcified plasma to which optimal amounts of thromboplastin have been added as determined by the method of Quick. The normal time varies between eighteen and twenty-four seconds, depending on the activity of the thromboplastic material employed.

THE VITAMIN USED: ITS POTENCY

Vitamin K is perhaps best defined as a fat-soluble substance a deficiency of which in the diet of young chicks results in an abnormal tendency of these animals to bleed. Its exact chemical composition is unknown and the only available preparations for clinical use represent nothing but biologically tested concentrates of this antihemorrhagic material and perhaps other substances.

In our [1a] earlier experiments, concentrates of vitamin K prepared from putrefied fish meal were used. These were effective in the prevention and control of cholemic bleeding. The material used during the past one and a half years was prepared in cooperation with the Abbott Laboratories from alfalfa meal extracted with petroleum ether; from the final product, chlorophyll and certain other pigments have been removed by adsorption. The preparations have a potency of 20 mg. or less per kilogram of chick diet as measured by Dann's modification [12] of the Almquist method. Two hundred mg. of the crude concentrate was approximately equivalent to 66 Gm. of dry alfalfa meal and was estimated to contain about 37,500 Dam units. These measures of unit value are obviously of limited value and cannot be evaluated properly until vitamin K has been isolated in pure form.

11. Almquist, H. J., and Klose, A. A.: The Isolation of Vitamin K as a Choleic Acid, J. Am. Chem. Soc. **61**: 745-746 (March) 1939.
12. Dann, F. P.: Vitamin K Assays, Am. J. Physiol. **123**: 48-49 (July) 1938.

DOSAGE AND METHODS OF ADMINISTRATION OF VITAMIN K

The minimal requirements and exact dosage of vitamin K necessary for the control of the hemorrhagic diathesis of jaundiced patients must await the further chemical purification and isolation of vitamin K. Eventually, these considerations will doubtless depend on the duration of jaundice, the degree of hepatic injury and the state of hypovitaminosis present.

Oral Administration.—Depending on the individual patient, the daily dosage has varied from 200 mg. to 8 Gm. of the crude concentrate. As much as 20 Gm. of the latter material has been administered by mouth for a period of seven days without the appearance of any untoward reactions; 13 Gm. of the crude concentrate mixed in peanut oil has been administered intramuscularly for a period of four days without harmful effects.

For purposes of routine preoperative treatment, we have divided our jaundiced patients into three groups: (1) those who have a normal prothrombin time, (2) those who have a prolonged prothrombin clotting time without active bleeding and (3) those who have a prolonged prothrombin clotting time with active bleeding.

Those jaundiced patients of the first group who have a normal prothrombin time have nevertheless been administered prophylactic treatment for from two to five days before surgical intervention is undertaken. From two to six gelatin capsules (each capsule containing approximately 200 mg. of alfalfa concentrate), together with from 1 to 4 Gm. of animal bile salts, seems to constitute an adequate daily dose. Almost any type of animal bile salts can be used, but we have preferred water-soluble bile salts, particularly in those instances wherein concentrates of vitamin K must be administered by means of a duodenal tube or T tube. Human bile obtained from a biliary fistula or a T tube as previously described by us [1a] or lyophilized bile as described by Johnston [13] may also be employed.

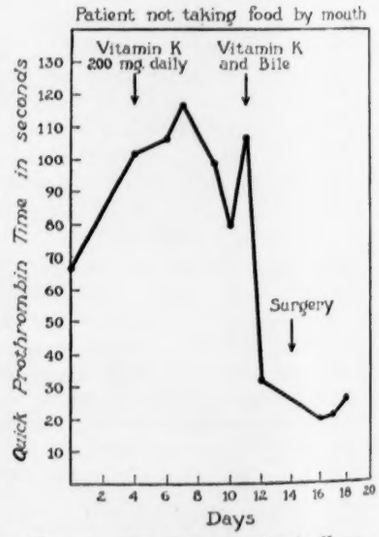

Chart 2.—The effects of vitamin K concentrates alone and in combination with bile on the prothrombin clotting time of a patient suffering from complete acholia, taking no food by mouth. Note that no effect was obtained until bile was administered.

Those patients having jaundice who have an elevated prothrombin time constitute a potential or real emergency and have been treated as such. Most patients having a prothrombin time of from thirty to forty-five seconds will respond well to the plan of prophylactic treatment previously mentioned, but if the prothrombin time is longer than forty-five or fifty seconds it has been thought advisable to administer concentrates of the vitamin together with bile salts either by duodenal tube or through a T tube. In such instances from 2 to 4 Gm. of a water-soluble bile salt is dissolved in from 250 to 500 cc. of warm

13. Johnston, C. G.: Preoperative and Postoperative Treatment in Cases of Obstructive Jaundice, Surgery **3**: 875-883 (June) 1938.

physiologic solution of sodium chloride or tap water; to this is added from 1 to 2 Gm. of the concentrate of alfalfa containing vitamin K. The mixture is shaken thoroughly and administered slowly in from thirty to sixty minutes by the drip method; care is taken to keep the solution warm and well mixed. One such dose, as a rule, will bring the prothrombin clotting time to a normal value. In the exceptional instance it has been necessary to repeat this procedure one or more times. When large or repeated doses are used, the prothrombin time usually decreases within six to twelve hours.

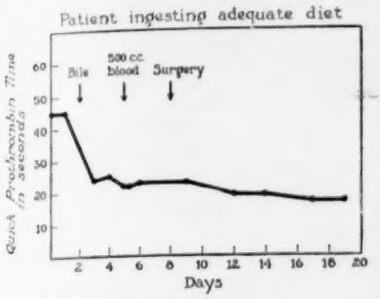

Chart 3.—The effect of human bile obtained from a biliary fistula on the prothrombin clotting time of a patient who was ingesting an adequate diet.

The problem of treatment of patients who are actively bleeding is difficult. Clotted blood must be removed by lavage before adequate absorption of the vitamin can occur, and not infrequently gastric lavage and irrigation of drainage tubes leading from the biliary tract are required. A transfusion of blood often is necessary to aid in combating the shock produced by hemorrhage and to provide a temporary supply of prothrombin; a transfusion will as a rule control bleeding only so long as the added supply of prothrombin lasts, a matter of from six to twelve hours. Rhoads and Panzer [14] suggest that "bank blood" is low in prothrombin and is therefore of little value in controlling hemorrhage in these cases. Treatment with the vitamin concentrate and bile salts is carried out in the meantime as described in the preceding paragraph and repeated as necessary.

Intramuscular Use of Vitamin K.—Parenteral administration of vitamin K has been used by Dam and Glavind [15] for a total of eight patients having obstructive jaundice. Emulsions of concentrates of alfalfa containing vitamin K were administered by the intramuscular route; such injections were followed by a diminution in the elevated R [16] values (coagulation times) in their patients. The responses obtained were not conspicuous until from five to seven days had elapsed. Similar results were obtained in chickens with elevated R values produced by ligation of the choledochus following a single intracardial injection of vitamin K concentrate. Greaves [17] has found concentrates of vitamin K to be effective in the rat when administered either subcutaneously or intraperitoneally.

We have administered intramuscularly to patients concentrates of alfalfa containing vitamin K mixed with peanut oil; this has been given in single doses varying from 200 to 3,200 mg. of the crude concentrate. There was little immediate change in the elevated prothrombin time following the daily injection of amounts up to 2,000 mg. The most satisfactory response was obtained in the treatment of a patient having a stricture of the common bile duct of two and one half years' duration. A total of 3.2 Gm. of crude concentrate mixed with peanut oil was given intramuscularly on four successive days. The effect on the prothrombin time is shown in chart 1. We have had a few patients whose elevated prothrombin times have decreased following the intramuscular injection of vitamin K, but in the main the effects have not been striking.

THE ABSORPTION OF VITAMIN K FROM THE DIGESTIVE TRACT

The Influence of Bile on Absorption.—It was demonstrated early that concentrates of fish meal, together with bile salts, were effective in controlling the hemorrhagic diathesis of patients having jaundice; the next consideration was to determine the effect on this condition of vitamin K and bile salts administered separately. Results of this investigation have been reported previously by us.[18] We administered daily doses of 200 mg. of fish meal concentrates for seven days to a patient who had complete acholia and who was taking no food by mouth. No effect was noted and the prothrombin time continued to rise; it dropped rapidly, however, following the administration of bile and vitamin K together (chart 2). This result illustrates clearly the failure of absorption of the fat-soluble antihemorrhagic material when bile is absent from the intestine. This observation has been confirmed by the experimental work of Greaves and Schmidt [18] and of Heymann,[19] who have demonstrated independently the importance of bile in the absorption of other fat-soluble vitamins from the intestinal tract.

The remaining consideration was to determine the effect on the prothrombin time of bile alone. It has previously been shown that normal and acholic feces have a definite protective effect on K-avitaminous chicks, indicating that the vitamin is normally present in the intestine (Butt and Osterberg [20]). A patient who was ingesting an adequate diet was given 250 cc. of fresh human bile obtained from a biliary fistula; within twenty-four hours the elevated prothrombin time had decreased to a near normal figure (chart 3). Similar results have been obtained independently by Warner and his associates.[2]

These clinical experiments have been confirmed recently in the experimental laboratory. Greaves [21] has demonstrated that bile is essential to the absorption of vitamin K by the rat and that, in animals subsisting on a K-deficient diet, bile alone has no effect on the hemorrhagic tendency, whereas vitamin K plus bile salts is immediately effective.

The Importance of a Normal Intestinal Surface for Absorption.—It is obvious that normal absorption of a fat-soluble material from the intestine cannot take place unless an adequate and physiologically intact intestinal surface is available. That deficiency in the concentration of prothrombin can develop because of disease of the intestinal tract has not hitherto been demonstrated, so far as we are aware. Recently we have had the opportunity of observing a group of patients suffering from K-avitaminosis which resulted apparently from an inadequate intake of food, abnormal or insufficient intestinal absorptive surface, or both.

14. Rhoads, J. E., and Panzer, Lillian M.: The Prothrombin Time of "Bank Blood," J. A. M. A. **112**: 309-311 (Jan. 28) 1939.
15. Dam, Henrik, and Glavind, Johannes: The Clotting Power of Human and Mammalian Blood in Relation to Vitamin K, Acta med. Scandinav. **96**: 108-128, 1938.
16. The term R value as used above describes the relation of the clotting time as determined by Fisher's method to that of normal blood (Dam and Glavind [15]).
17. Greaves, J. D.: Studies on the Vitamin K Requirements of the Rat, Am. J. Physiol. **125**: 429-436 (March) 1939.
18. Greaves, J. D., and Schmidt, C. L. A.: The Role Played by Bile in the Absorption of Vitamin D in the Rat, J. Biol. Chem. **102**: 101-112 (Sept.) 1933.
19. Heymann, Walter: Metabolism and Mode of Action of Vitamin D: IV. Importance of Bile in the Absorption and Excretion of Vitamin D, J. Biol. Chem. **122**: 249-256 (Dec.) 1937.
20. Butt, H. R., and Osterberg, A. E.: Distribution of Vitamin K in Biologic Material and Its Probable Physiologic Significance, abstr. J. Nutrition (supp.) **15**: 11 (June) 1938.
21. Greaves, J. D.: The Nature of the Factor Which Is Concerned in Loss of Blood Coagulability of Bile Fistula and Jaundiced Rats, Am. J. Physiol. **125**: 423-428 (March) 1939. Greaves.[17]

REPORT OF CASES

CASE 1.—A markedly debilitated male patient who had chronic ulcerative colitis and who presented other evidence of nutritional deficiency underwent resection of the colon; several days later the patient was found to be bleeding freely from a tube which had been inserted into the small intestine. The prothrombin clotting time was forty-six seconds. Concentrates containing vitamin K were administered at once by way of the enterostomy and on the following day the bleeding ceased. The prothrombin time had decreased to twenty-six seconds.

CASE 2.—A boy suffering from multiple polypi of the transverse and descending colon and rectum had suffered from multiple attacks of intestinal obstruction with resulting loss in weight and strength. Excision of the left half of the transverse and descending colon had been performed following preliminary ileosigmoidostomy. Shortly thereafter partial intestinal obstruction developed, which persisted for a period of twenty-eight days; there was an intervening period of three days during which the obstruction was spontaneously relieved. After unsuccessful attempts to relieve the obstruction by intestinal intubation, enterostomy was finally done. Forty-eight hours later, blood began to drain freely from a tube which had been inserted into the small intestine. The prothrombin time was found to be greatly prolonged (151 seconds). Vitamin K concentrates and bile salts were administered through the enteric stoma, resulting in an immediate decrease in the prothrombin time to the normal value, cessation of bleeding and eventual recovery.

CASES 3 and 4.—Two cases of chronic ulcerative colitis were studied. The first patient, who had a high iliac stoma, had a prothrombin level of 67 per cent (as measured by the method of Warner). There had been no bleeding other than that associated with the primary disease. The second patient was bleeding freely from the enteric stoma and the prothrombin clotting time was forty-four seconds. Bleeding was controlled for this patient by the administration of concentrates of vitamin K and bile salts, and the prothrombin time decreased to twenty-four seconds.

TABLE 1.—*Diagnoses in Sixty-Four Cases of Jaundice of Various Types, Previously Reported*

Diagnosis	No.	Patients Bleeding
Carcinoma, head of pancreas	21	7
Stricture, common bile duct	15	4
Stone in common bile duct	13	2
Cirrhosis of liver	7	0
Carcinoma of bile ducts	4	1
Acute and subacute cholecystitis with stones; associated hepatitis	3	0
External biliary fistula	1	0
Total	64	14
Diagnoses in Sixty-Three Cases Representing New, Unreported Cases of Jaundice		
Acute and subacute cholecystitis with stones; associated hepatitis	16	4
Stricture of common bile or hepatic ducts	13	1
Carcinoma, head of pancreas	11	1
Stone in common bile duct	11	1
Carcinoma, bile ducts	7	1
Cirrhosis of liver; hepatitis	5	0
Total	63	8
Grand total	127	22

CASE 5.—A male patient having a gastrojejunocolic fistula of two years' duration had on admission a prothrombin clotting time of sixty seconds; a quantitative estimation of prothrombin produced low values (9 to 12 per cent). No bleeding had occurred at any time. Combined intramuscular and oral administration of vitamin K concentrates corrected the deficiency in prothrombin; the prothrombin time decreased to thirty seconds and the quantitative content increased to 48 per cent.

CASES 6 and 7.—Two cases of nontropical sprue were studied. The first patient had a content of fat in the stools of 40 per cent (dry weight). The fat content of the stools of the second patient was 33 per cent (dry weight). The level of prothrombin in the circulating blood as measured by the method of Warner was definitely reduced (47 per cent and 62 per cent of normal, respectively). No hemorrhagic tendencies had been noted as afflicting either patient. Fatal hemorrhagic diathesis may occur in the presence of sprue; the occurrence probably depends on K-avitaminosis and prothrombin deficiency. Fanconi [22] recently has reported that in the presence of celiac disease of children there is, because of the abnormal absorption of fat, an abnormal tendency to bleed. He noted the existence of hypothrombinemia in such cases and a prolonged coagulation; he has suggested that this "skorbutoid" tendency might be caused by a deficiency of vitamin K. Engel [23] has made a similar suggestion.

TABLE 2.—*Effect of Preoperative and Postoperative Administration of Vitamin K in 127 Cases of Jaundice* *

When Administered	Patients Treated	Patients Who Bled After Operation
Before and after operation	73	5 (7%)
Before operation only	32	2 (6%)
After operation only	22	14 (64%)

* Sixty-four of these cases have been reported previously.

While cases of prothrombin deficiency referable to defects in intestinal absorption are not often encountered, they do comprise a rather distinct group and one which bears further investigation. When hemorrhage of patients having extensive disease of the intestine occurs either before or after surgical treatment, deficiency in prothrombin should be excluded before other forms of treatment are instituted. The optimal site of absorption of vitamin K in the intestinal tract is not as yet known; Dixon and Clark [24] at the Mayo Clinic are now investigating the problem. The material is taken up rapidly from the jejunum, as has been previously mentioned, but it does not seem to be absorbed from the stomach or colon.

THE ROLE OF THE LIVER IN THE UTILIZATION OF VITAMIN K

In the preceding paragraphs the presence of bile in the bowel and a normal intestinal surface are proved to be of importance in the absorption of vitamin K and in maintaining a normal concentration of prothrombin. An equally important factor, the integrity of the hepatic parenchyma, remains to be considered. The liver is assumed to be the site of formation of prothrombin, as indicated by the studies of Smith and his associates.[25] They demonstrated the important role of this organ in the formation of prothrombin in their studies on dogs suffering from intoxication with chloroform. If hypoprothrombinemia is accepted as being the principal factor responsible for the hemorrhagic tendency of patients having jaundice, it may reasonably be assumed that in many such instances the element of hepatic parenchymal damage has a distinct bearing on the condition. Actually, even a badly damaged liver is capable of synthesizing prothrombin; we have records of patients who presented every known clinical evidence of hepatic insufficiency and who have exhibited maximal degrees of physiologic disturbance (as determined by studies of

22. Fanconi, G.: Zöliakie, Deutsche med. Wchnschr. **64**: 1565-1568 (Oct. 28) 1938.
23. Engel, Rudolf: Sprue und Vitamin-K-Mangel, Med. Welt, No. 4, Jan. 28, 1939, p. 120.
24. Dixon, C. F., and Clark, R. L.: Personal communication to the authors.
25. Smith, H. P.; Warner, E. D., and Brinkhous, K. M.: Prothrombin Deficiency and the Bleeding Tendency in Liver Injury (Chloroform Intoxication), J. Exper. Med. **66**: 801-811 (Dec.) 1937.

hepatic function) who have been able to absorb and utilize vitamin K and maintain normal values for the concentration of prothrombin in the blood. However, within the past year we have encountered, as has Warner,[26] certain patients having severe hepatic damage who did not present the usual prompt response in prothrombin clotting time following the administration of vitamin K. In one instance the patient showed no response whatever.

RESULTS OF VITAMIN K AND BILE SALT THERAPY

Concentrates of vitamin K prepared from alfalfa, together with animal bile salts, have been administered to 127 patients suffering from jaundice of various types who were subjected to various surgical procedures; ninety-five (75 per cent) of these had obstructive jaundice subsequently. Sixty-four of the cases represented by these 127 patients have been reported previously.[1b] The diagnoses for these 127 patients and the number of patients in each diagnostic group who bled are presented in table 1. The frequency with which the hemorrhagic state develops in these patients is apparent.

For a large majority of these patients, bleeding has been adequately controlled by the administration of concentrate of vitamin K and bile salts; typical responses are illustrated in charts 5 and 6. There are some patients for whom this treatment must be regarded as a failure, a matter which will be discussed subsequently.

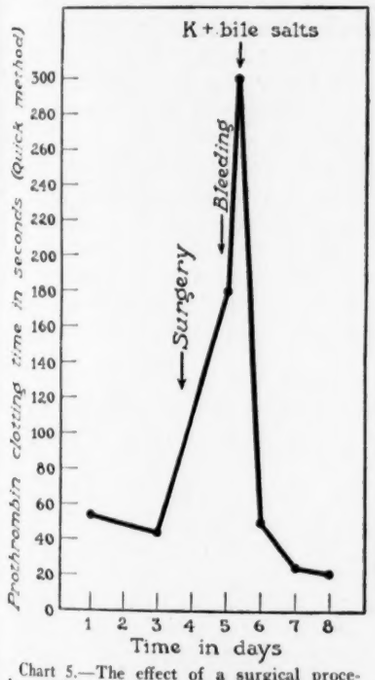

Chart 5.—The effect of a surgical procedure on the prothrombin clotting time; actual bleeding was controlled and a greatly prolonged prothrombin clotting time was reduced to normal by the administration of vitamin K concentrates and bile salts.

In analyzing the data pertaining to these two groups of patients, the most unexpected finding was the considerable frequency with which bleeding afflicted individuals suffering from acute and subacute cholecystitis with stones and various degrees of hepatitis. It has been well established that cholemic bleeding occurs with the greatest frequency in those patients in whom bile is completely excluded from the gastrointestinal tract for long periods, and hemorrhagic diathesis which afflicts a patient having long-continued neoplastic obstruction thus occasions but little surprise. In this series the bleeding of patients having carcinomatous obstruction as a rule was recognized early and was adequately treated. Unfortunately, relatively little attention has been paid to the danger of the postoperative bleeding of patients who have gallstones and hepatitis. As a result, there were numerous unexpected episodes of hemorrhage in this group of patients.

26. Warner, E. D., in discussion on Butt, H. R.; Snell, A. M., and Osterberg, A. E.: Oral and Intramuscular Administration of Vitamin K in Hemorrhagic Diathesis of Obstructive Jaundice, abstr. J. A. M. A. **112**: 879-880 (March 4) 1939.

We have learned that a normal prothrombin clotting time on the day of operation does not guarantee the nonoccurrence of postoperative bleeding and that close attention to the risk of hemorrhage is warranted in the treatment of all patients who have obstructive jaundice and hepatic damage arising from whatever cause.

In the hepatic parenchyma of a number of patients suffering from advanced cholecystic disease, the surgeon at operation observes various gross changes. The finding of moderate or severe hepatitis in such instances

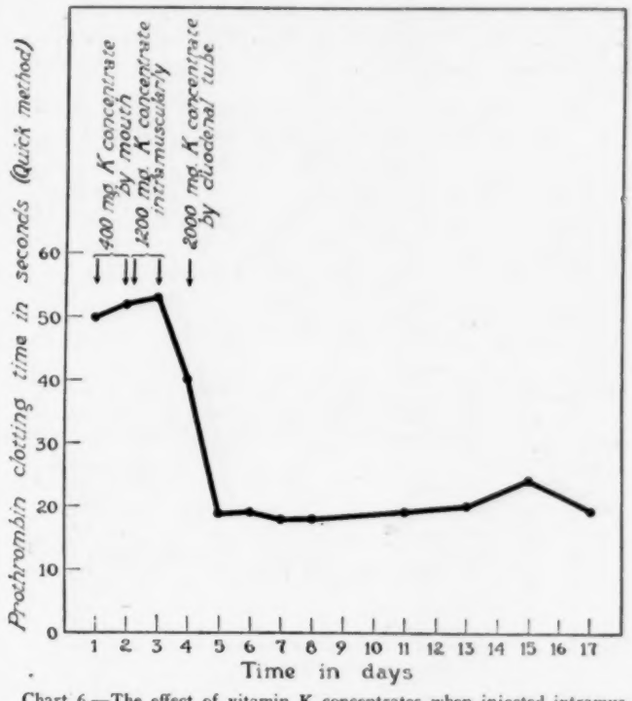
400 mg. K concentrate by mouth
1200 mg. K concentrate intramuscularly
2000 mg. K concentrate by duodenal tube
Prothrombin clotting time in seconds (Quick method)
60
50
40
30
20
10
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
Time in days

Chart 6.—The effect of vitamin K concentrates when injected intramuscularly and by duodenal tube on a prolonged prothrombin clotting time.

should constitute a warning that added precaution during the postoperative period is necessary. The integrity of the hepatic parenchyma may be a controlling factor in such instances, and because of this fact the importance of continuing all known methods of maintaining and improving hepatic function in patients having jaundice or hepatic injury cannot be overemphasized. The ready availability of vitamin K should not lull either the clinician or the surgeon into any false sense of security; the material should be employed in conjunction with other methods which are known to be of value in the restoration of normal hepatic function.

THE VALUE OF PREOPERATIVE TREATMENT

The value of the preoperative administration of vitamin K is well illustrated by an analysis of the sixty-three recently studied cases mentioned in an earlier paragraph. Of eight patients to whom no concentrate of vitamin K or bile salts was given before surgical intervention, bleeding occurred postoperatively in five (63 per cent). This incidence of bleeding is about sixteen times greater than the incidence of postoperative bleeding in the group of forty-five patients to whom concentrates of vitamin K and bile salts were given both before and after surgical intervention; of the two patients (4 per cent) of this group who bled, one had only a slight oozing of blood from the T tube and the other patient had pyloric obstruction of a degree which precluded successful treatment. Vitamin K concentrates

and bile salts were administered to ten patients before but not after operative procedures. Only one patient bled to a serious extent, and this patient had received inadequate amounts of vitamin K before surgical treatment. The analysis of these sixty-three recently studied cases is very similar to that of the group previously reported by us; figures for the combined groups are represented in table 2. The importance of preventive or preoperative measures in the treatment of this group of patients is paramount and, as Elvehjem has stated in another connection, the time to treat deficiency states most advantageously is that at which they are detectable by laboratory means rather than that at which clinical symptoms are apparent.

CLINICAL INTERPRETATION AND USE OF THE PROTHROMBIN CLOTTING TIME BEFORE AND AFTER SURGERY

It must be assumed that present methods for measuring the content of prothrombin in the circulating blood are subject to considerable error. These methods are indirect and, as may be said of many other helpful laboratory procedures, they do not always produce all the information desired. We have observed what we believed to be cholemic bleeding afflicting two patients having normal prothrombin times; in each instance the bleeding was controlled by the administration of vitamin K. In all other instances wherein cholemic bleeding occurred, the prothrombin clotting time was at least twice the normal value or higher; however, we have notes of several patients who had a prothrombin time of from sixty to ninety seconds, yet these patients exhibited no gross evidence of bleeding. The decrease in the concentration of prothrombin in the circulating blood necessary to produce bleeding in man seems to depend on certain unknown individual factors; it certainly bears no constant relationship to the type of hepatic or biliary disease present. Very rapid changes in the coagulating properties of blood have been repeatedly noted in this series of patients.

TABLE 3.—*Prothrombin Clotting Time Obtaining in Conditions Associated with Abnormal Tendency to Bleeding*

No. of Cases	Diagnosis	Prothrombin Time (Seconds)*
3	Menorrhagia	19, 22, 25
2	Metrorrhagia	22, 19
5	Hemophilia	20, 22, 25, 20, 23
4	Essential thrombocytopenic purpura	21, 21, 24, 22
3	Toxic purpura	21, 23, 22
2	Essential hematuria	21, 19
2	Banti's syndrome	21, 19
2	Uncomplicated hemolytic icterus	26, 18
1	Familial bleeding tendency	25
1	Aplastic anemia	24
5	Hemorrhagic duodenal ulcer	24, 23, 26, 22, 21

* Method of Quick and his associates.

The prothrombin time of patients having jaundice usually increases to some extent for the first three or four days after surgical operation, but it may increase rapidly even as late as the eighteenth postoperative day. For this reason the prothrombin time should be determined daily for the first four days after operation and then every other day for at least eight or ten days longer. Any increase in the prothrombin time should constitute an indication for the immediate administration of a concentrate of vitamin K and bile salts by mouth or by duodenal tube. To those patients whose prothrombin clotting time before surgical treatment has been high, it is perhaps wise to administer the vitamin and bile salts daily for several days after surgical operation, regardless of the prothrombin clotting time. A patient who has a prothrombin clotting time of more than thirty seconds should be prepared with particular care and one who has a prothrombin time of more than forty-five seconds must be considered as a potential bleeder and treated as such.

THE USE OF VITAMIN K AND THE PROTHROMBIN CLOTTING TIME IN OTHER CONDITIONS ASSOCIATED WITH AN ABNORMAL TENDENCY TO BLEED

The effectiveness of vitamin K in the treatment of the hemorrhagic diathesis of jaundice has prompted an investigation of its possible application in other hemorrhagic states. We have determined the prothrombin clotting time in a number of conditions which are associated with an abnormal tendency to bleed. These conditions are listed in table 3, together with the results of our determinations. In this series of cases the prothrombin clotting time has been normal in each instance. Concentrates of vitamin K and bile salts have been administered in the treatment of several patients having hemophilia, menorrhagia, metrorrhagia and essential hematuria, and in no instance was the normal prothrombin clotting time or coagulation time altered, nor was the tendency to bleed affected appreciably.

Dam and Glavind [3] in 1938 reported normal "R values" in patients having thrombopenia, aplastic anemia, hemophilia and myeloma; Dam and his associates [27] in 1937 were unable to lower the coagulation time of a patient suffering from hemophilia after the administration of large amounts of vitamin K. Burch and Meade [28] have reported a case of multiple retinal hemorrhages of unknown causation which appeared to show improvement following administration of an oil extract of hemp which possessed vitamin K activity. Similar treatment had little or no effect on the retinitis which is associated with diabetes. The observations of Burch and Meade have not as yet been confirmed.

SUMMARY

Evidence is presented which indicates that the deficiency in prothrombin associated with the hemorrhagic diathesis of obstructive jaundice can be controlled by certain fat-soluble materials present in alfalfa. Although this material, vitamin K, must for the present be considered an empiric remedy, its biologic activity in man and animals can hardly be questioned. The control of a deficiency of prothrombin depends on several factors: (1) a normal diet containing the antihemorrhagic vitamin, (2) the presence of adequate amounts of bile salts in the intestine, (3) a normal intestinal absorptive surface and (4) a physiologically normal liver.

In a majority of patients suffering from jaundice, the second and fourth factors may be impaired singly or, more usually, in combination, as the foregoing paragraphs indicate. The routine methods of treatment suggested in this report may become obsolete when vitamin K is available in pure form or when it is possible to administer this vitamin by the parenteral route. No matter which method eventually may be employed,

27. Dam, Henrik; Schönheyder, Fritz, and Lewis, Liese: The Requirement for Vitamin K of Some Different Species of Animals, Biochem. J. **31**: 22-27 (Jan.) 1937.

28. Burch, E. P., and Meade, J. R.: Treatment of Hemorrhagic Retinitis with the Antihemorrhagic Vitamin: Preliminary Report, Minnesota Med. **22**: 32-33 (Jan.) 1939.

the importance of anticipating the danger of prothrombin deficiency and detecting it by means of laboratory studies will remain a paramount consideration in successful treatment.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. SMITH, ZIFFREN, OWEN AND HOFFMAN AND DRS. BUTT, SNELL AND OSTERBERG

DR. I. S. RAVDIN, Philadelphia: My experience with the use of materials containing vitamin K began in October 1937, when my associates and I began to use desiccated spring grasses with bile salts. Rhoads has recently reported our results. They are in general similar to those which we have just heard. Twelve years ago we reported that in the absence of a serum protein deficiency there was no deficiency in the serum calcium in obstructive jaundice. Rhoads and Warren have been studying the prothrombin content of the plasma under conditions of liver injury similar to these Dr. Smith and his co-workers have used, and the data are in agreement with theirs. In addition, they have studied the prothrombin content of the plasma of completely hepatectomized dogs and it is their opinion, as it is I am sure of the authors this morning, that the liver is probably the sole source of synthesis of prothrombin. Some of the failures to obtain satisfactory results have no doubt been due to inadequate doses of the vitamin containing substrate and to inadequate amounts of a potent bile salt preparation. Until available evidence is obtained in which substrates containing vitamin K can be accurately assayed, it is important that large doses, even overdoses of K substrates, be given, and this is true also of the bile salt preparations. Many of the bile salt preparations now available are relatively inadequate. The occasional unfavorable result which has been obtained even when large amounts of K-containing substrates and bile salts are administered is, as a rule, due to extensive liver injury. Every attempt should be made to improve the functional capacity of the liver prior to operation and to preserve its integrity after operation. I believe that, in addition to the use of substrates containing vitamin K and bile salts in this operative period, the diet of the individual should be such that the liver is conditioned against minimal injury as the result of operation and anesthesia. Such diet contains not only adequate carbohydrate but adequate protein. A liver high in fat and low in protein is maximally susceptible to injury. A liver low in fat and high in available protein is maximally resistant to such injury. It is important, therefore, that attention be paid not only to the vitamin K and bile salt requirements of these individuals but to the dietary factors which condition the degree of liver injury that may occur after the use of volatile anesthetics.

DR. JOHN D. STEWART, Boston: I have been interested recently in the phenomenon of fall in concentration of prothrombin following operation. In a group of nineteen patients operated on for obstructive jaundice an average postoperative drop in prothrombin concentration of 23 per cent was found. This is expressed in absolute percentage. The drop was maximal within three days. In these operations the various anesthetics used were procaine block and spinal and ether anesthesia, and no correlation was found between the type of agent and the extent of depression in prothrombin. On the other hand, patients without liver disease undergoing such operations as herniorraphy, total hysterectomy and combined abdominoperineal excision of the rectum showed an average drop of less than 5 per cent in prothrombin concentration after operation. Therefore, as yet I am inclined to regard the postoperative depression of prothrombin in obstructive jaundice as an expression of the reduction in prothrombin reserves. There is need in the clinical application of this subject for a simple, accurate method of determining the concentration of prothrombin, and also a need for a purified form of vitamin K which can be given parenterally, possibly obviating the need for giving bile salts. Dr. Smith and his co-workers have supplied us with an accurate two stage method of determining the prothrombin. This bedside method should be used widely and frequently. I was interested in the observation of Dr. Butt and his co-workers that they have encountered patients with the hemorrhagic diathesis in obstructive jaundice without reduction in the prothrombin concentration. It has been my lot to see ten patients with massive bleeding in obstructive jaundice, eight of them after operation, and in no case has the prothrombin level been above 40 per cent. I should like to ask Dr. Smith whether he has studied the extent of fluctuation of prothrombin in normal individuals over a period of time. I should like to ask Dr. Butt whether, in the study of various clinical conditions, he has encountered abnormal increase in the plasma prothrombin level.

E. A. DOISY, PH.D., St. Louis: Owing to the earlier work of Dam and Almquist, my associates and I have been in the fortunate position of being able to continue the biochemical work on vitamin K. Several months ago we isolated the first pure vitamin K. Shortly after that we isolated a second compound which likewise was pure and crystalline and which also possesses vitamin K properties. The first compound obtained was from putrefied fish meat. It is a solid at room temperature, a light yellow, crystalline salt. The second compound, obtained from alfalfa, is a light yellow oil at room temperature. However, it has been recrystallized a great many times at lower temperatures. Some of the important points mentioned today have been the preparation of a material which can be used parenterally. I don't believe we are now in a position to report that, but we have plans under way which I think will lead to such a preparation. Some of the speakers have been hopeful of obtaining definite indication of the amount of vitamin K to be used. That is within our grasp now that we have the crystalline material. It would be wise in the near future to do away with bile assay procedures and adopt the use of the pure compound. Moreover, if the bile assays are to be continued, it would probably be wise to adopt some permanent crystalline stable compound as a base standard, such as the League of Nations has done with a great many of the hormones and vitamins. Within the last few weeks we have attained such a compound. Vitamin preparations are notoriously unstable for alkali and light. The new compound we have seems to be a great deal more stable and perhaps is entirely stable toward light. Consequently, that will afford us a definite base standard for the assay, if assays must be continued.

J. D. GREAVES, PH.D., St. Louis: During the last ten years I have carried out experiments which indicate that bile salts are essential, at least in the rat, to the normal intestinal absorption of not only vitamin K but also vitamins D, E, B-carotene and, to a lesser extent, vitamin A. Only, however, in the case of vitamin K has a clearcut clinical deficiency been demonstrated in the clinical patient. This might seem strange, but a glance at the conditions associated with vitamin K deficiency adequately explains the discrepancy. Most fat soluble vitamins are stored in large amounts in the body and held in reserve for times of need. This is not the case with vitamin K. But small amounts of this factor have been found in the various tissues of the body. The animal or patient when placed on a deficient diet is soon depleted and deficiency symptoms show up. Furthermore, this finding is consistent with the rapid and dramatic fluctuation seen in the prothrombin levels of the patient as well as the experimental animal. The patient with biliary disease usually selects a low fat diet, low also in fat soluble vitamin factors. In the presence of complete obstruction, bile does not enter the intestine, with the result that the whole of the dietary supply is cut off. Liver injury adds an additional complication. Even after relief of the jaundiced condition the quantity and quality of the bile produced by the liver are inadequate. All these factors superimposed accentuate the deficiency, and the patient develops the hemorrhagic tendency reported by Dr. Butt. It must be remembered that potentially the body is also deprived of its supply of the other fat soluble factors when bile is removed from the intestinal tract. However, it seems that in this case the body reserves are usually adequate to meet the body's needs during the time of the deficiency. In our work on the influence of jaundice and liver poisons on the utilization of carotene and vitamin D we have found that liver damage results in faulty utilization of these factors. A similar observation has been made with vitamin K recently in bile fistula animals in which secondary complications resulted in marked liver damage. Such animals have failed to respond to even large doses of vitamin K concentrates. These observations confirm Dr. Butt's observations. Dr. Butt pointed out that we had

found the administration of vitamin K subcutaneously or orally to be effective in the relief of the deficiency symptoms of the bile fistula and jaundiced rat; however, a very large dosage of a quite highly purified material was administered; even then the parenterally administered material was not as effective as was a much smaller amount administered orally with bile salts.

DR. G. V. LEROY, Chicago: These papers on the clinical usage of vitamin K are of great interest. One is reminded of the fact that the deficiency was first discovered in an analysis of the bleeding tendency in chicks which occurred unassociated with trauma. Hematologists tend to separate the bleeding diathesis into two portions: Disturbances of the coagulation mechanism, an example of which is hemophilia. Disturbances in the mechanism which maintains the integrity of the capillary wall, an example of which is scurvy in which hemorrhage occurs independent of trauma in patients whose coagulation mechanism is apparently normal. Mixed forms are perhaps demonstrated by essential purpura. The first group has prolonged coagulation time and normal bleeding time. The latter group has the reverse. The vitamin K deficiency appears to be a mixed state. Study of this deficiency has been carried out mostly in terms of prothrombin, which is concerned with the coagulation mechanism. I would enjoy hearing any of the authors discuss the effect of vitamin K on capillary fragility, and the role, if any, of altered capillary fragility on the clinical state associated with deficiency of that vitamin.

DR. H. P. SMITH, Iowa City: Dr. Stewart asked regarding normal variations in prothrombin level. We have made determinations on normal laboratory workers and have found that the variation is rarely more than 15 per cent. In ward patients having minor illness the variation is somewhat greater. However, these patients often do show some malnutrition, and this may be important. The question of capillary fragility is perhaps of great importance in certain diseases but probably not in the jaundiced bleeder. We too have found that some patients who fail to respond to the ordinary dose of vitamin K and bile salt will respond promptly to increased dosage. One patient whose prothrombin remained low despite the usual dosage of vitamin and bile did respond promptly when the dose of bile was increased fivefold. I think we shall have to guide our therapy, as Dr. Butt suggested, by the use of prothrombin tests. I am convinced that the requirements both of vitamin K and of bile salt, vary markedly from case to case. It is encouraging to hear the results of Dr. Doisy and to know that we are going to have in the near future purified material with which to work. The various commercial products now available vary tremendously, and their potency is largely unknown.

DR. HUGH R. BUTT, Rochester, Minn.: In answer to the question by Dr. Stewart concerning the abnormal increase in the level of prothrombin following administration of concentrates of vitamin K, we have given as much as 20 Gm. of the crude concentrate of alfalfa together with bile salts by mouth over a period of two or three days or as much as 13 Gm. of the crude concentrate of alfalfa mixed with peanut oil by the intramuscular route without any untoward reactions and without any abnormal increase above the normal level of the prothrombin in the blood. Concerning the effect of concentrates containing vitamin K on ordinary laboratory coagulation and bleeding times, in the past the experience among surgeons indicated that coagulation and bleeding times as determined by standard methods are altered little until the patient is on the very brink of bleeding or is actively bleeding. Finally, laboratory tests, such as those developed by Dr. Quick and his associates and by Dr. Smith and his associates, enable us to detect early an apparent nutritional deficiency and make early treatment possible. As Dr. Elvehjem has said in another connection, the time to treat deficiency states is when they are detected by laboratory procedures rather than awaiting the appearance of definite clinical symptoms. I should like to stress the importance of not relying too strongly on any single determination of the level of prothrombin. A blood may appear to be normally coagulable but within a few hours it may become virtually incoagulable. Those who have followed many of these patients have had the opportunity to see the terrible misfortune that can happen by depending too much on any laboratory procedure. A question which I think is most important has already been stressed by Dr. Ravdin. The normal level of prothrombin is little affected following operation in patients with normal liver function or with minimal injury to the liver. However, patients who have slightly more than the minimal liver damage or, as usually is the case, have much liver damage, are markedly affected by anesthetics and by surgical procedures, and these patients bear the most careful attention in preventing cholemic bleeding during the postoperative period.

RABIES IN BIRMINGHAM, ALABAMA

HUMAN MORTALITY AS AFFECTED BY ANTIRABIES TREATMENTS

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In this paper we deal with the experiences of a local health department in the prevention of rabies among human beings. We are especially concerned with those problems which confront the physician; namely, the value of antirabies vaccine and indication for its administration.

The difficulties involved in maintaining continuous programs for the enforced confinement of dogs, along with the failure to find other effective control measures, has greatly intensified the problem of rabies. Through failure to control the dog, increased reliance has been placed in secondary control measures. Antirabies vaccine has been administered to an ever increasing number of persons who become exposed to an ever increasing number of rabid dogs.

TABLE 1.—*Rabies Data of Birmingham, Ala., for 1938*

	Total	White	Negro
Population*	256,203	152,677	103,526
Dogs owned*	20,609	13,012	7,597
Dogs per family	0.31	0.32	0.28
Rabid animals submitted by	245	214	31
Human treatments	640	576	64
Human deaths	0	0	0

* By 1938 census.

The original Pasteur treatment and its several modifications have become generally accepted as reasonably safe and highly effective in preventing rabies among human beings. This, together with the ready availability of the vaccine, the ease of its administration, the morbid fears of a misinformed public regarding the disease, the apparent 100 per cent mortality among those actually infected and untreated and the general failure on the part of responsible parties to limit treatment to those for whom it is definitely indicated, are all factors which commonly lead to the indiscriminate administration of vaccine.

In epidemic areas the attitude of the public is a real handicap to the medical adviser, for there is probably no disease about which the public is more misinformed. The fears, horrors and superstitions of the exposed individual, magnified by a superabundance of bad advice obtained from well meaning friends, often produce a state of panic before a physician is reached. Circumstances of exposure so infinitely remote as to make the

possibilities of infection ridiculous and unworthy of even momentary consideration often cause such extreme mental anguish that nothing short of vaccine treatment can prevent nervous collapse of the individual. "Undue apprehension" is probably as common a symptom among the many recently exposed persons as it is among the very few who develop the disease clinically. Under such circumstances the individual is often unable or unwilling to accept medical advice and insists on vaccine treatment, while the physician too often fails to maintain a professional attitude and allows himself to be influenced by the undue apprehension of the patient.

INCIDENCE OF RABID ANIMALS IN BIRMINGHAM AND IN ALABAMA

The incidence of rabies in Alabama has been variously reported.[1] During the seventeen year period 1922 to 1939 a total of 11,218 animals have received a positive laboratory diagnosis of rabies, 42,947 individuals were given antirabies vaccine and forty-eight persons died of the disease.

Birmingham has been considered by some as the "rabies capital" of North America and possibly of the civilized world. Further, the incidence of the disease in the surrounding county of Jefferson is not materially less than in the corporate limits of the city.

Birmingham, located in north central Alabama, covers an area of 54 square miles. It is essentially industrial and largely devoted to the manufacture of iron products and building materials. The health department has divided the city into fifty-two census tracts, which average a square mile in area and about 5,000 in population. Census figures for both human and dog populations were determined in 1938 by actual survey made as a WPA project under supervision of the health department (table 1). The total population of 256,203 is 40 per cent Negro. The dog census enumerated 20,609 dogs for which ownership was established. The actual number is much higher, as it was obviously impossible to count ownerless strays.

During the last ten years (1929 to 1939) in Birmingham (table 2) a total of 1,495 animals have received a positive laboratory diagnosis of rabies, 5,206 persons received antirabies vaccine and three persons died of the disease. Since 1931 the number of known rabid animals has not dropped below 100 annually except in 1935, when effective control measures were temporarily enforced. In Jefferson County, which includes Birmingham, the incidence from year to year has varied markedly though the general trend is definitely upward; 1938 constituted the year of maximum incidence with a total of 443 known rabid animals. In Birmingham alone in 1938 slightly more than 1 per cent of the owned dog population was known to have developed rabies. This increase is actual and is based on the larger number of animals examined each year as well as a steady increase in the percentage of positive observations. The indicated rise in rabies here is quite evidently a true one and represents a deepening of the animal reservoir of this infection.

As incredible as these figures may appear, they do not express the true prevalence. They represent largely the incidence of rabies among pets of those persons intelligent enough to suspect the disease and interested enough to bring the animal heads to the laboratory. Failure of dog owners to recognize clinical symptoms, which frequently are atypical, and the tendency of rabid animals to leave their home environment result in failure even to suspect many animals. Negroes are too unconcerned and too uninformed to suspect rabies. During 1938 in Birmingham only thirty-one, or 12.5 per cent, of 245 rabid animals were submitted to us by Negroes despite the fact that Negroes constitute 40 per cent of the population and are known to have almost as many dogs per family as white persons (table 1).

Further illustration is afforded by a study of the various census tracts as shown in table 3. If the data from these tracts are assembled on the basis of dog ownership, it is found that in those areas where Negroes own from 75 to 100 per cent of all dogs the reported incidence of rabies is lowest (0.5 per cent) but becomes progressively higher (to 1.5 per cent) as the percentage of white owned dogs increases. This, of course, represents incompleteness of data, not true incidence.

The almost total disregard of rabies by Negroes is again shown by studies undertaken to determine the effectiveness of prophylactic canine vaccination. Negroes in Birmingham vaccinated 10 per cent (799) of their dogs during 1938 and of these not one was found rabid. On the other hand, white persons vaccinated 40 per cent (5,107) of their dogs and of these 0.5 per cent (twenty-six) were submitted for examination and found rabid. Obviously the effectiveness of canine vaccination does not depend on the color of the dog owner, and such a difference in the reporting of vaccine failures represents neglect on the part of the Negro to seek a diagnosis of animals either killed or dying of disease.

TABLE 2.—*Prevalence of Rabies in Birmingham, Ala.*

Year	Total Animal Heads Examined	Number Positive	Per Cent Positive	Individuals Treated	Human Deaths
1929.....	219	83	37.9	318	..
1930.....	173	60	34.7	346	1
1931.....	321	182	56.7	643	1
1932.....	402	205	51.0	841	..
1933.....	284	145	51.0	555	1
1934.....	471	178	37.8	793	..
1935.....	202	61	30.2	201	..
1936.....	241	104	43.1	309	..
1937.....	401	232	57.9	560	..
1938.....	397	245*	61.7	640	..
Total.....	3,111	1,495	48.0	5,206	3

* Including nineteen micronegative, mouse positive examinations.

RELATION BETWEEN HUMAN MORTALITY FROM RABIES AND THE ADMINISTRATION OF ANTIRABIES VACCINE

The data presented are sufficient to indicate that the prevalence of rabies among dogs in Alabama generally, and in Birmingham in particular, is sufficiently great to constitute a potential danger of high degree to the human population. One might expect human deaths from rabies to be frequent but, as a matter of fact, they are quite unusual. The exact reason for this is not clear, but the following facts show that it is by no means entirely due to the wholesale and indiscriminate administration of vaccine.

During the past seventeen years 42,947 persons received antirabies vaccine in Alabama with a mortality from rabies of only 0.06 per cent. This low rate, according to the usual interpretation of treatment statistics, constitutes a very favorable showing for effective

1. Denison, George A.: Rabies: Prevalence, Treatment, Control, J. M. A. Alabama, March 1935. Baker, J. N.; McAlpine, J. G., and Dowling, J. D.: Rabies: A Continuing Challange, South. M. J. **29**: 547-557 (June) 1936. Denison, McAlpine and Gill.[2]

treatment. But perhaps of greater significance is the fact that of the forty-eight persons who died of rabies during the same period, twenty-three, or 48 per cent, were judged to have received prompt [2] and adequate treatment.[3] The persistence with which fatalities continue to be equally distributed among the treated and untreated affords ground for wide speculation.

The Alabama State Health Department distributes Semple vaccine without charge to physicians for the treatment of those exposed to rabid animals. The department also pays a nominal fee to the physician for the administration of vaccine to each indigent person. Since July 1933 detailed questionnaire forms have accompanied each treatment, and to January 1939 some 10,000 of these forms, representing 44 per cent of all treatments issued for the same period, have been returned and studied. A summary of the facts contained therein is given in table 4.

These data show that the dog is the principal animal involved, and experience indicates that the dog is directly responsible for the spread of the disease to those other animals which were responsible for the remaining treatments. A high percentage (62.1) of animals to which treated individuals were exposed received either a clinical or a laboratory diagnosis of rabies. The extremely high percentage of exposures of the upper extremities greatly exceeds that reported by McKendrick [4] and is the result not only of bites but of indirect exposure through handling animals with or without cuts or abrasions on the hands. Actually 43.3 per cent of all persons on whom information is available took treatment without having been bitten. Negroes seldom take treatment unless bitten and in fact took only 10 per cent of all treatments administered; yet they suffered only fourteen fatalities as compared to thirty-four fatalities in the white population.

The population of Alabama, according to the 1930 census, is 64 per cent white and 36 per cent Negro. The rate at which white persons take vaccine treatment is five time that for Negroes for all types of exposure and four times that for Negroes when only actual bites are considered. Expressed in another way, these data would indicate that, if the 3,000,000 people in Alabama were all white, and the same ratio of treatments prevailed, one could expect an increase of 40 per cent in the number of treatments issued per annum with no significant change in mortality. Likewise, if the 3,000,000 people in Alabama were all Negroes we would expect a 72 per cent decrease in treatments with no significant change in mortality.

TABLE 3.—*Dog Ownership in Relation to Apparent Incidence of Rabies at Birmingham, Ala., for 1938*

Per cent Negro owned dogs....	75-100	50-74	25-49	10-24	5-9	Under 5
Number of census tracts.....	12	10	7	11	6	5
Number of dogs inventoried...	4,177	3,620	2,406	4,992	2,458	2,956
Number of known rabid dogs.	22	25	31	73	37	44
Per cent of known rabid dogs.	0.5	0.7	1.3	1.5	1.5	1.5

Data for racial distribution of treatments and fatalities from rabies are practically the same for Alabama, Birmingham and Jefferson County. In Birmingham we have more complete collateral information on which to judge their meaning. For example, in Birmingham we know that (1) Negroes have practically as many dogs per family as white persons (table 1). Their animals are subject to the poorest of care, and Negroes undoubtedly are bitten and otherwise exposed to rabies as often as the white persons; (2) Negroes submit only one seventh as many rabid animals to the laboratory as do white persons; (3) the rate at which Negroes take treatment is only one sixth that of the white population, and (4) during the ten year period of study Negroes suffered only two deaths from rabies and white persons only one. It is remarkable that, in an area where the risk of exposure appears so great, the Negro population can so completely ignore rabies without disaster.

TABLE 4.—*Antirabies Treatments in Alabama* *

	Number	Per Cent	Total Returns on Which Data Are Based
Dog, biting animal	9,494	85.6	11,098
Laboratory or clinical diagnosis of rabies on biting animal	6,692	62.1	10,769
Location of exposed part			7,885
Head	478	6.1	
Trunk	143	1.8	
Arm	5,312	67.3	
Leg	1,958	24.8	
Persons "exposed" but not bitten	3,506	43.3	8,093
Treatment distribution by race	.....	....	11,176
White	10,056	90.0	
Negro	1,120	10.0	

* Analysis of questionnaires from July 1933 to January 1939; types of exposure among those receiving vaccine.

In the experiences cited there is little relation between mortality from rabies and the administration of antirabies vaccine, for (1) among the highly exposed untreated (Negro) population fatalities are no greater than among the highly exposed treated (white) population, and (2) such rare fatalities as do occur are equally distributed among the treated and the untreated. An explanation of these data should probably assume a high degree of resistance to natural infection in the vast majority of both races and an occasional failure of either natural resistance or vaccine treatment to protect when infection is massive or well placed or when for some unknown reason individuals may be peculiarly susceptible. It is not inferred from this that vaccine is without value but rather that its value has been greatly exaggerated. This exaggeration is largely the result of the inclusion in treatment records of large numbers of individuals who, although definitely exposed to risk, would not have developed the disease, and also by the inclusion of many others whose exposure to risk was too insignificant even to warrant vaccine treatment.

ADVISABILITY OF TREATMENT (BIRMINGHAM PROCEDURE)

Recognition of these factors in Birmingham has led to the adoption of a more rigid procedure regarding treatment. A concerted effort is made to limit the administration of vaccine to those most probably infected by direct exposure.

The frequent attitude of the public toward treatment was expressed at the beginning of this discussion. The attitude of perhaps the majority of physicians was quite well expressed in a recent article [5] which stated that

2. Starting within seven days following exposure. Twenty-four were treated, but for one treatment was delayed three weeks.

3. Denison, George A.; McAlpine, J. G., and Gill, D. G.: Rabies Deaths in Alabama, Am. J. Pub. Health **27**: 869-874 (Sept.) 1937.

4. McKendrick, A. G.: Seventh Analytical Review of Reports from Pasteur Institutes on the Results of Antirabies Treatment, Quart. Bull. Health Organ., League of Nations, Geneva **6**: 1 (Feb.) 1937.

5. Blatt, Maurice L.; Hoffman, Samuel J., and Schneider, Maurice: Rabies: Report of Twelve Cases with a Discussion of Prophylaxis, J. A. M. A. **111**: 688-691 (Aug. 20) 1938.

"antirabies vaccine should be administered to any person bitten by, or contaminated in any way by the saliva of an animal known to be rabid." Both attitudes are expressions of failure to evaluate the risk of exposure or the risk of treatment complications and reflect an unwillingness to assume responsibility.

In Birmingham all vaccine is distributed by the bureau of laboratories of the health department, and in every case careful scrutiny is made of the exposure history. Individuals making direct application are advised and if treatment is necessary are referred to their physician of choice. However, the majority of individuals seen at the health department are those sent in by physicians for advice. Such advice regarding treatment is communicated to the physician, who makes final disposition of the case. Vaccine is released only on the verbal or written order of the physician, and usually only after the merits of the individual case have been freely discussed between the physician and the laboratory director.

Disposition of the Animal.—Whether the animal appears normal or sick, it should be quarantined for a period of from ten to fourteen days. If typical symptoms of rabies develop, the treatment need not be further delayed. Confirmation of diagnosis, however, should be made at autopsy. If death occurs within the period of observation, early microscopic examination of the brain is made. If positive, treatment is begun. If negative, the clinical symptoms of the animal must be taken into consideration in an effort to arrive at a diagnosis. The importance of clinical observation is apparent when the limitations of direct microscopic examination for Negri bodies is appreciated. Leach [6] has determined the presence of rabies virus in brain material by both mouse inoculation and direct microscopic examination. He reports positive mouse tests for 12 per cent of brains on which Negri bodies were not found by direct microscopic examination, and negative mouse tests among 0.9 per cent of brains on which Negri bodies were reported as found by experienced technicians.

In endemic areas such as Birmingham every dog that bites should be considered rabid until known to be otherwise. When the condition of the animal is unknown because it cannot be located or cannot be positively identified or the laboratory examination is unsatisfactory, it is advisable to administer treatment to those bitten.

These procedures are quite generally followed in Alabama with apparent safety. In Birmingham treatment ordinarily is delayed until the animal has died and the diagnosis has been established. Face bites and multiple bites are, of course, excepted.

Actual Bites or Scratches.—For actual bites or scratches made by the teeth or claws, treatment is always advisable. In the case of bites above the shoulders or multiple severe lacerations of the body or extremities, treatment should be started immediately but may be discontinued later if the animal proves not to be rabid. In some instances it is probably safe to wait from tweny-four to forty-eight hours if the history of the dog is known and if it can be observed by an experienced veterinarian; but, unless the animal remains perfectly normal, treatment should not be further delayed. For other bites it is safe and usually desirable to delay treatment until a definite diagnosis can be made either clinically or by laboratory procedure.

Complete reliance in the effectiveness of antirabies vaccine is never justified, and cauterization of wounds made by the animal with strong nitric acid is necessary for adequate protection of the patient. There is no substitute for nitric acid; mercurochrome and agents which coagulate the tissues are worthless. If areas of heavy nerve distribution are involved, the use of nitric acid is all the more imperative. In ten years' experience we have seen only one wound that had received proper local treatment.

Other Exposures Requiring Treatment.—The point to emphasize is that treatment is usually advisable only following an actual bite or scratch made by the suspected animal. Other extenuating circumstances, of no great importance, sometimes warrant treatment as, for example, the known contamination of fresh open wounds with saliva. Such an exposure assumes the importance of a bite only if there is some abrading force to carry the saliva into the wound. The wound itself is of importance only if it was of sufficient size to have been easily noticed, and provided it had been made on the day of the exposure to the animal. It is not felt that the mere handling of rabid animals with fresh open cuts on exposed parts is important unless there is direct contamination with saliva and, unless such contact is known to have occurred, treatment is not advised.

When infants and young children have had intimate contact with rabid animals for extended periods of time, treatment may be advisable, especially if the parents are unobservant or ignorant of what may have transpired. Fifty per cent of deaths from rabies in Alabama occur in children under 13 years of age.

Treatment has occasionally been advised for highly nervous women, not for the prevention of rabies but to avoid nervous collapse or hysteria. Two such individuals were treated because of definite rabies psychosis.

When Treatment Is Not Advised.—Treatment is not advised following (1) contamination of old cuts, sores, abrasions, scratches or hangnails with saliva of known rabid animals; (2) "pinches" in which the skin is definitely broken but the clothing neither torn nor penetrated; (3) handling, eating after, sleeping with, kissing or other intimate exposure to rabid animals; (4) drinking milk of rabid cows, eating meat of rabid animals; (5) bites of any animal living fourteen days from the time of biting; (6) bites from fleas from rabid animals; (7) any exposure to a case of human rabies other than an actual bite, or direct contamination of fresh open wounds, or (8) any exposure of an nonrabid animal just bitten by a rabid animal except when infected saliva is directly transmitted to a fresh open wound.

While, theoretically, rabies can be contracted from these and many other types of exposure, it practically never occurs. Vaccine paralysis, or other serious complications resulting from administration of vaccine, are probably more frequent than the development of rabies from any exposure other than an actual bite; and, in advising treatment one should carefully weigh the possibilities of death or permanent injury from vaccine against the possibilities of death from rabies.

Four known paralytic accidents have occurred in Alabama with the administration of 33,147 Semple treatments, an incidence of one in 8,287. Of the forty-

6. Leach, Charles N.: Comparative Methods of Diagnosis of Rabies in Animals, Am. J. Pub. Health **28**: 162-166 (Feb.) 1938.

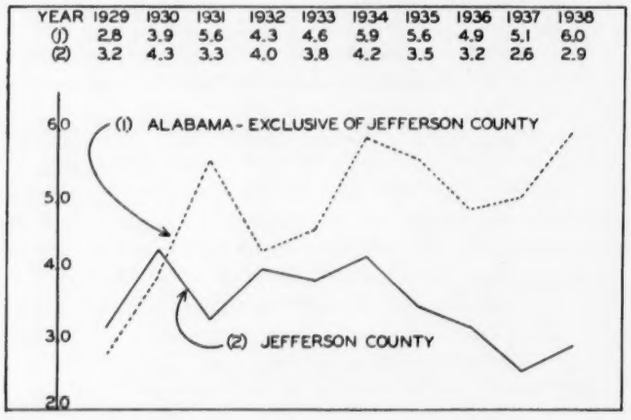
five [7] deaths in Alabama on which there is definite history regarding the type of exposure, all the victims are known to have been bitten. These two facts contain the whole wisdom of withholding treatments from those not actually exposed.

The following histories of exposure, for which treatment was administered in Alabama, were taken from questionnaire forms. They are selected to illustrate conditions for which treatment would not have been advised in Birmingham:

1. No known exposure, treatment given as a safeguard.
2. Bathed in water which was used in washing a child that had been bitten by a rabid dog.
3. Treated wounds of child, no contact with rabid animal.
4. Saliva from rabid animal got in hair.
5. Handled clothing of grandson who played with rabid dog.
6. Patient had wound on finger when washing out tub from which rabid cow drank water.
7. Dressed chicken which had been killed by rabid dog.
8. Had small abrasions of hands and handled chain with which rabid animal was tied.
9. Drank milk from rabid cow.
10. Milked cow that was rabid.

The following histories of contact with known rabid animals are characteristic of many for which treatment

YEAR	1929	1930	1931	1932	1933	1934	1935	1936	1937	1938
(1)	2.8	3.9	5.6	4.3	4.6	5.9	5.6	4.9	5.1	6.0
(2)	3.2	4.3	3.3	4.0	3.8	4.2	3.5	3.2	2.6	2.9



Average number of treatments per known rabid animal.

was not advised and not administered in Birmingham. These summaries are taken from records of exposure for May and June 1938:

1. A bottle used to give medicine to a rabid dog was discarded and was immediately picked up by a baby, who placed the mouth and neck of the bottle in its mouth.
2. Handling and petting rabid dog, also kissing.
3. Individual claiming to have a gastric ulcer drank milk of a rabid cow.
4. Had hands in mouth of rabid dog; briar scratch and barbed-wire cut on hands made the day before.
5. Handled and drenched rabid calf throughout its illness. No cuts or scratches on hands.
6. Handled dog about mouth and head. Had scratches on hand which were not made by the animal.
7. Mechanic had small fresh cuts and abrasions on hands. Handled rabid dog about head while transporting animal in automobile.
8. Had hands in mouth of rabid dog trying to remove "bone from throat." No visible cuts or abrasions at the time.
9. Six members of a family handled rabid dog throughout illness. None were bitten or scratched by animal, all had minor abrasions on hands.
10. Handled rope with which rabid dog was tied, handled dog's head after its removal from carcass. Had superficial fresh abrasions on hands.

If the indications for and against the administration of treatment, as given in this discussion, appear to depart considerably from all accepted procedures, it should be remembered that they have been followed in Birmingham for the past ten years in advising approximately 10,000 individuals, as yet without a fatality.

It is not intended to imply that all lay persons and physicians in Jefferson County follow this advice. On the contrary, only about one third to one half of them do. Nevertheless it is felt that some reduction in the useless administration of vaccine has been accomplished. The accompanying chart correlates by year the average number of Semple treatments given for each known rabid animal for Alabama (exclusive of Jefferson County) with the same information for Jefferson County. Treatments for the latter are considerably lower and show a more definite downward trend than in the remainder of the state. This has been accomplished without an increase in mortality.

A word of warning should be directed to those who may wish to follow the procedures outlined in advising treatment. The problems of the exposed individual should never be viewed with contempt. No matter how remote the contact with an infected animal may appear, a careful history is essential to eliminate the possibility of real exposure. Only after careful consideration is a decision justified.

SUMMARY

The incidence of rabies among animals in Birmingham, Ala., has steadily risen during the past ten years. The increase is actual and is based on the larger number of animals examined each year, as well as a steady increase in the percentage of positive observations. The problem appears to be largely one of unconfined, home owned dogs (pets); very few unidentified animals are received for examination. The year's total of rabid dogs approximates 1 per cent of the known dog population. This figure is largely made up of dogs submitted for examination by white owners and would probably be doubled if Negroes were equally cautious.

During a period of ten years, 5,206 vaccine treatments were administered to human beings. While Negroes constitute 40 per cent of the population, they submitted only 12.5 per cent of all rabid animals, took only 10 per cent of all treatments and, like the white population, suffered only a rare mortality. Figures for the state as a whole substantiate these data. There appears to be little relation between mortality from rabies and the administration of vaccine.

The Birmingham procedure recommends treatment only for those quite definitely exposed to rabid animals.

CONCLUSIONS

The data presented are not of a type to warrant definite conclusions. The following general statements are offered as implicit in the experience cited:

1. Rabies is primarily a veterinary problem. Regardless of its prevalence among dogs, it will probably never cause sufficient morbidity or mortality among human beings in this region to allow its classification as a public health problem of importance.

2. If rabies were as easily contracted by man as is commonly supposed, it would in Alabama become one of the leading causes of death. Instead, it continues to be a very rare disease.

7. Of the remaining three deaths in the state no information regarding exposure is available and nothing is known except that one victim was a child of 3 years, one a man of 63, a stranger in the community about whom little was known; one was a man of 80 who developed rabies two days after "doctoring" a rabid dog, but he unquestionably received his infection at least several weeks earlier.

3. In this region there appears to be little relation between mortality from rabies and the administration of antirabies vaccine.

4. Aside from an actual bite or scratch, circumstances of exposure rarely warrant vaccine treatment.

5. When considering the advisability of treatment for exposures other than an actual bite, the possibilities of vaccine paralysis or other serious complications should be considered.

6. The problem of rabies, as it is known in Birmingham, appears to be one of home owned dogs (pets) and not of unidentified strays.

SPERM EXAMINATION ACCORDING TO THE PRESENT STATE OF RESEARCH

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The examination of semen as it is generally done is quite inadequate. Usually the contents of the condom are examined for (1) semen fibers and (2) mobile semen fibers and the number of mobile semen fibers is roughly computed.

Owing to the recent research by Macomber and Sanders, Mönch, Stiasny and Generales, Michael, and Joël and Pollák, the exact obstructions to fecundity in a man can be ascertained.

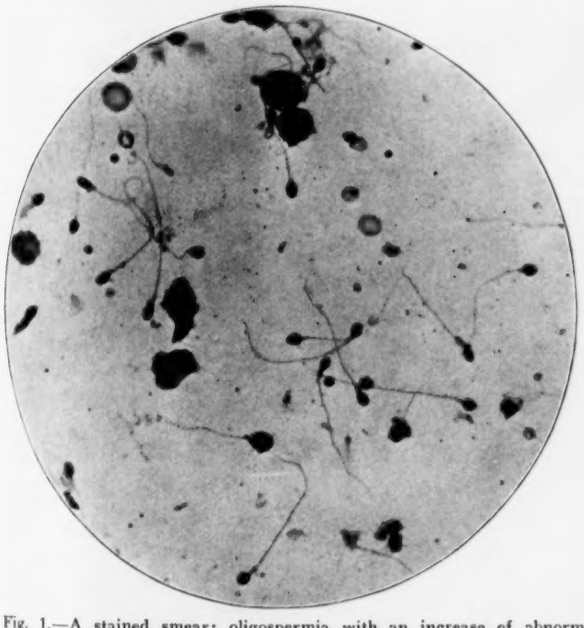


Fig. 1.—A stained smear; oligospermia with an increase of abnormal sperms (16 per cent) and cells (20 per cent).

There are three conditions to be observed in investigation of the sperm:

1. The examination should be preceded by a pause in ejaculation of from four to seven days at least. Only one ejaculation should take place in order to provide material for examination.

2. The material should if possible be obtained by the physician through auto-erotic manipulation or coitus interruptus. The contents of the condom are unsuitable, and other ways of obtaining material are inadequate.

3. The material should be examined within thirty to sixty minutes. Graduated vials are suitable for eventual transport. The material is to be protected against high temperatures.

History taking and clinical examination should always precede sperm examination. Attention should be paid to (1) family history, including the physical

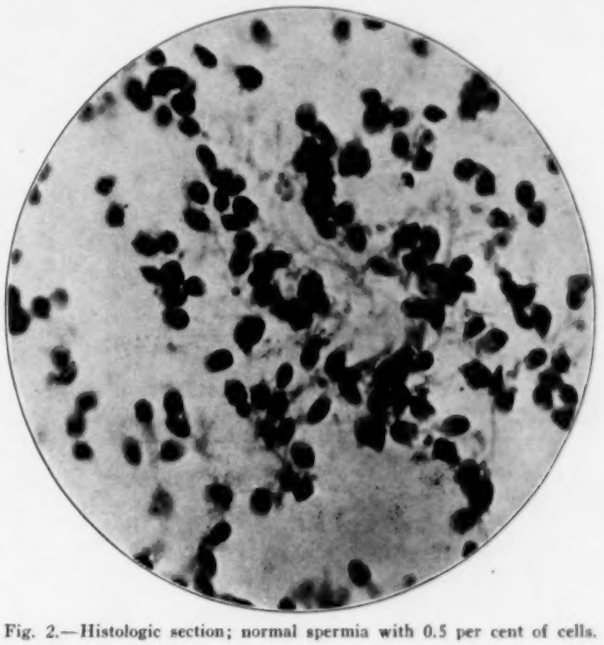


Fig. 2.—Histologic section; normal spermia with 0.5 per cent of cells.

and mental condition and the profession of the parents, grandparents, brothers and sisters of both the husband and the wife; (2) the personal history, including former diseases such as parotitis, tuberculosis, syphilis, gonorrhea, rheumatism and mental diseases, as well as accidents, and (3) the sexual history, including all particulars of the sexual life of the husband and wife before, in and outside their marriage, obtained first in separate interviews and then in a mutual interview, the duration of their marriage and the number and nature of the cohabitations being investigated.

The clinical examination concerns the type of constitution, the mental and physical health and, especially, the primary and secondary sex characteristics.

After having obtained all these facts, part of which are included in the examination report, we proceed to the macroscopic examination of the ejaculate. This concerns:

1. The quantity, which normally amounts to from 3 to 5 cc. (average, 3.3 cc.) under the conditions mentioned. Smaller quantities (about 0.5 cc.) usually are pathologic, whereas larger ones are not.

2. The consistency of the fresh ejaculate. This is of a specially gelatinous character but when exposed to fresh air changes in from ten to thirty minutes. The partly liquefied, somewhat slimy fibrous ejaculate containing white flakes is then examined. An originally thin ejaculate is usually poor in semen fibers, whereas a thick ejaculate, which does not liquefy readily, often is pathologic.

3. Color and smell. These will be noticed only in pathologic specimens.

Because definite conclusions cannot be drawn from the macroscopic investigation alone, the microscopic investigation is actually more important.

After the ejaculate is liquefied we make a preliminary preparation. The ejaculate is well mixed with a fine

glass capillary tube and a drop put on an object-bearer. This may be covered or, when a concave object-bearer is used, regarded as a hanging drop. If no sperms are found after repeated examination, the ejaculate should be thoroughly centrifuged. In case of extreme oligospermia it is necessary to concentrate the material. If this method does not produce the desired result, it is necessary to examine colored smears, because sometimes slime-covered sperm cannot be distinguished in the original preparation. When all these examinations have a negative result, then and only then may one speak of azoospermia. Azoospermia is a condition in which one cannot find sperms but there are more or less ripe cells of spermiogenesis. In aspermia, however, one can find neither sperms nor cells.

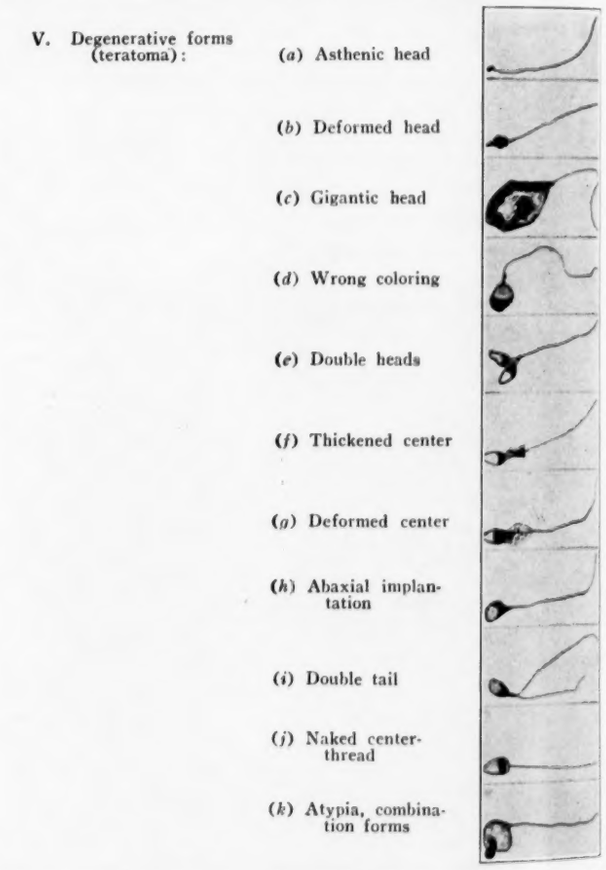
TABLE 1.—*Spermiogram According to Pollák and Joël, I-IV*

I. Normal spermatozoon
II. Physiologic variations: (a) Round head
(b) Narrow head
(c) Rejuvenated head
(d) Small head
(e) Large head
III. Youthful forms (unripe spermatozoon): (a) Cytoplasm rest at the head
(b) Cytoplasm rest at the center
IV. Aged forms (overripe spermatozoon): (a) Vacuoles
(b) Hyperpigmented
(c) Depigmented

To determine the number of sperms the ejaculate is mixed thoroughly by means of a capillary tube and drawn up to the 0.05 mark of an erythrocyte-mixing pipet. A diluting fluid is then drawn up to the 1.01 mark, the most suitable fluid being physiologic solution of sodium chloride to which has been added carbolfuchsin 0.1 cc. to 100 cc. The mixture is well shaken and a Thoma-Zeiss counting chamber filled. The counting is repeated twice in order to obtain results as accurate as possible. Sixteen large squares (i. e. $16 \times 16 = 256$ small squares) are to be counted. In the calculation we divide by 256 to obtain the number to a small square, multiply according to the dilution by 200 and according to the chamber measures by 400,000 (one small square amounts to 0.0025 cu. mm. and the chamber depth to 0.1 mm.). The formula is now: $n \times 200 \times 400{,}000/256 = m$ (n is the number of sperms to sixteen large squares and m is the number of sperms per cubic centimeter). Normally the number of sperms in 1 cc. varies between 60 and 120 millions. Higher numbers (hyperspermia) are generally not pathologic, and lower numbers (hypospermia or oligospermia) are detrimental to the prognosis.

The number of motile sperms is determined by means of the Ehrlich ocular screen, which divides the field of vision into four quadrants. Given the aforementioned conditions, especially when examination takes place within thirty to sixty minutes after the material is obtained, normally at least 80 per cent of all semen fibers are motile. We use the terms normokinesis, hyperkinesis and hypokinesis to express the degree of motility, whereas we express the number of motile sperms in percentages of the aggregate of semen fibers. A decline of the motile sperms usually accompanies a decline of the degree of motility. This condition is called asthenospermia.

TABLE 2.—*Spermiogram: V. Degenerative Forms (Teratoma)*



When no motile sperms are found, we try to call forth motility. As actual necrospermia is very rare, stimulating efforts are often successful. In most cases in which no motile semen fibers are found, one is dealing with suspended animation, a latent akinesis, an immobilization. Our stimulating efforts with isotonic solutions of magnesium salts change the image essentially. We make the solution by mixing 8 parts of a 5.42 per cent dextrose solution with 2 parts of an eighth normal solution of magnesium hydroxide, magnesium chloride or magnesium sulfate. A glass capil-

lary tube 12 or 15 cm. long and 1 mm. in broad diameter is marked lengthwise at 1 cm. and at 10 cm. The thoroughly mixed ejaculate is drawn up to the first mark and the diluting solution to the second mark. The contents are mixed by drawing up and blowing out the contents twice. Then we transfer the solution to the cavity of a concave object-bearer. The cavity is filled

TABLE 3.—*Spermiogram: VI. Cells of Spermiogenesis*

entirely, air bubbles should be avoided and the whole is covered with a covering glass. The preparation is observed under the microscope for ten minutes. If we do not perceive any movement within this time, we speak of necrospermia. In case of failure the experiment is repeated. We make use of the same experiment in cases in which there are a large number of akinetic sperms or in cases of high grade hypokinesis. Under the influence of the magnesium solutions we often improve the original results.

In a special laboratory we can perform resistance experiments, using hypertonic and isotonic solutions. For hypertonic solutions we use 15 per cent hydrochloric acid, 0.5 per cent acetic acid and 70 per cent alcohol, and for isotonic solutions we use eighth normal sodium hydroxide and eighth normal sodium carbonate in dextrose solution. The procedure is the same as that of the stimulating efforts. The capacity for resistance, which should be present in acids as well as in alkalis, can of course be measured only in normal or approximately normal motile sperms.

The examination of original preparations is followed by the examination of colored smears. An experienced observer may be able to discern differences in the shape and size of the sperms in the original preparation, but these stand out clearer in suprāvital coloring. By the addtion of one drop of 1 per cent watery solution of brilliant cresyl blue the motility of the sperms is influenced so slightly as to leave sufficient time for observation. One can judge the number of motile abnormally shaped sperms and the number of immotile normal sperms. Thus one is enabled to distinguish between natural and artificial products. This makes the observation of colored smears a great deal easier.

Colored smears are the most suitable for the differentiation of structures of sperms and of cells of spermiogenesis. The smears, which are prepared like blood smears, must be as thin as possible. They are dried in fresh air by fanning and are fixed and colored. One part of the preparation is colored with hemalaun [1]-eosin and the other with azur-eosin. The two stains complement each other, because the structure of the sperms is better visible with the first and the structure of the cells more easily distinguished with the second.

TABLE 4.—*Spermiogram: VII. Other Cells; VIII. Elements*

VIII. Elements:
(a) Prostate corpuscles
(b) Lecithin corpuscles
(c) Fat crystals
(d) Böttcher crystals
(e) Testicle cylinders

For coloring with hemalaun-eosin the preparation is fixed for two minutes with methyl alcohol, refixed for five minutes with 95 per cent and 70 per cent ethyl alcohol and then rinsed quickly in water. It is then

1. Hemalaun is similar to hematoxylin but not identical. It is a 2 per cent solution of crystalline hematin in 95 per cent alcohol 5 cc. and a 5 per cent aqueous solution of $KAl(SO_4)_2.12H_2O$ 100 cc.

colored for twenty minutes with hemalaun, steeped in running water for thirty minutes or, if possible, twelve hours, colored a second time for five minutes with fresh hemalaun, rinsed for ten minutes in water, colored for contrast for three minutes with a 3 per cent alcoholic eosin solution, differentiated in an alcohol sequence of 70, 90 and 100 per cent, cleared in carbol-xylene and embedded in Canada balsam under a covering glass.

For coloring with azur-eosin, the preparation is fixed for two minutes with methyl alcohol, colored for twenty minutes with a diluted Giemsa-Romanowski azur-eosin solution, rinsed in distilled water and embedded in Canada balsam under a covering glass. The coloring solution is prepared fresh each time; to 5 cc. of distilled water is added ten drops of the Giemsa-Romanovski solution.

The preparations are then examined by means of immersion, and at least 200 sperms and cells are counted. Normal ejaculates have 80 per cent of morphologically normal sperms and thus at the most 20 per cent of abnormal ones. The normal relation is from 0.25 to 2 cells of spermiogenesis to 100 ripe sperms. In cases of pathologic change, the number of abnormal sperms, the number of cells of spermiogenesis or both may be increased. The maximal pathologic numbers we have found are 86 per cent of abnormal sperms and 60 per cent of cells in the same case. With azoospermia one finds only cells. Besides sperms and cells of spermiogenesis, other cellular substances and elements are to be found. The other cells include macrophages, microphages, spermiophages, real and unreal giant cells, Sertoli cells, epithelium cells of the seminal and urinary tract, and leukocytes. The elements include

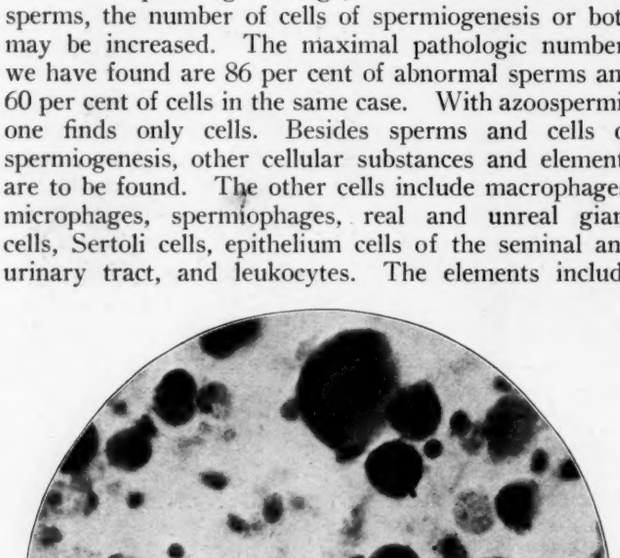


Fig. 3.—Histologic section; asthenospermia with 60 per cent of cells.

prostate and lecithin corpuscles, fat crystals, Böttcher crystals and testicle cylinders.

Using the works of Mönch and the spermiogram of Stiasny and Generales as a basis, we set up a new formula for practical use. The results of our experiments and experience have driven us to changes and far-reaching alterations in the spermiogram.

The histologic investigation finally completes the examination of the ejaculate. This enables one to study exactly the morphologic picture, the cell structures, to locate the trouble and to judge the nature of the trouble in the progress of the spermiogenesis. Our method offers special advantages in judging the therapeutic results, which show earlier with cells of spermiogenesis than with ripe spermatozoids. The embedding and coloring of sections is the work of a specialist and

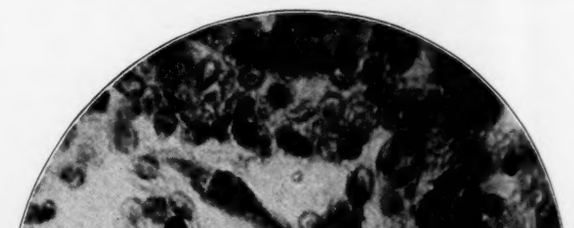


Fig. 4.—Histologic section: Sertoli cells (0.25 per cent); cells 20 per cent. These sections were exhibited at the fifth Congress of Cytologists at Zurich in August 1938.

therefore it is advisable to pour a 4 per cent solution of formaldehyde on the rest of the examined ejaculate and to submit this for the purpose of histologic research to the special laboratory.

With this method of examination it is possible to distinguish between azoospermia and aspermia, to limit the expressions necrospermia and asthenospermia, and to establish various diseases such as localized degenerative-regenerative processes in the testicle, testicular atrophy, testicular hypoplasia, abnormalities of the epididymis, especially after gonorrhea, and, finally, derangements in the distal part of the seminal-urinary tract. Thus it is possible to form a reliable opinion about the fecundity of a man.

Free Institutions and Scientific Progress.—Relative to the first decade of the century, progress has been striking, but due consideration of the many aspects of the subject convinces one that continued advance in science and industry cannot be maintained unless scientific methods and an enduring probity are practiced in the conduct of government, in the drafting and application of laws, and in the conduct of public business generally. . . . The presence of a relatively large number of enthusiastic and talented young scientific men in our universities is certainly one of the necessary factors for good progress, but this alone would have been insufficient to account for the American miracle. The factor of tremendous importance, perhaps even decisive, was indubitably the existence of our free institutions, financially independent and unhampered by centralized bureaucratic control. Their liberating influence over successive generations produced a type well suited to widening intellectual frontiers. Self reliance and resourcefulness probably came to be inherent characteristics in a people who have the stamina needed to settle a continent in a relatively short time. —Keyes, F. G.: *Science* **89**:209 (March 10) 1939.

REFLEX BILIARY DYSKINESIA RELIEVED BY APPENDECTOMY

REPORT OF THREE CASES

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AND
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There is a mass of clinical evidence establishing the relationship between true cholecystitis and appendicitis. The research of Rosenow [1] and the clinical observations of Heyd,[2] Deaver,[3] Mayo,[4] Latham and English [5] and Draper [6] are examples of the attention this relationship has received in the literature. Rivers and Hartman [7] found that 31.8 per cent of 879 patients operated on for true cholecystic disease had chronic or acute appendicitis, and Draper,[6] more recently, found that 40.6 per cent of his patients with operative cholecystitis and cholelithiasis had concomitant appendicitis.

In view of the clinical relationship between cholecystitis and appendicitis, it has been supposed that a diseased appendix may be the cause of a reflex disturbance in the biliary tract. Dyskinesia of the gallbladder and the sphincter of Oddi is now a well established clinical entity. Oddi,[8] Aschoff and Bacmeister [9] and Berg [10] were leaders in opening the field of the neurogenic origin of disturbances of the biliary tract. Westphal [11] gave perhaps the greatest impetus to the conception of functional and reflex disturbances of the biliary tract. His work has been both substantiated and elaborated on by Ivy,[12] Whitaker,[13] Ivy and Sandblom,[14] Greene, Twiss and Carter,[15] Best and Hicken [16] and Hill,[17] as well as many others.

The diagnosis of dyskinesia of the gallbladder rests on three definite observations, namely an irregular symptom complex of pain in the right upper quadrant or colic, nausea, distention, diffuse tenderness and vomiting; a cholecystogram showing a normally concentrating gallbladder with delayed evacuation, and biliary drainage showing a failure of the gallbladder to respond normally to stimulation with magnesium sulfate and olive oil.

A search of the recent American literature fails to reveal the report of an authenticated case in which dyskinesia of the gallbladder has been relieved by appendectomy.

References and case reports have appeared in the foreign literature claiming relief from biliary dyskinesia through the removal of a diseased appendix. Norsa [18] gave evidence of complete relief from pyloroduodenal spasm following appendectomy, with x-ray evidence of a return of normal pyloric and duodenal function.

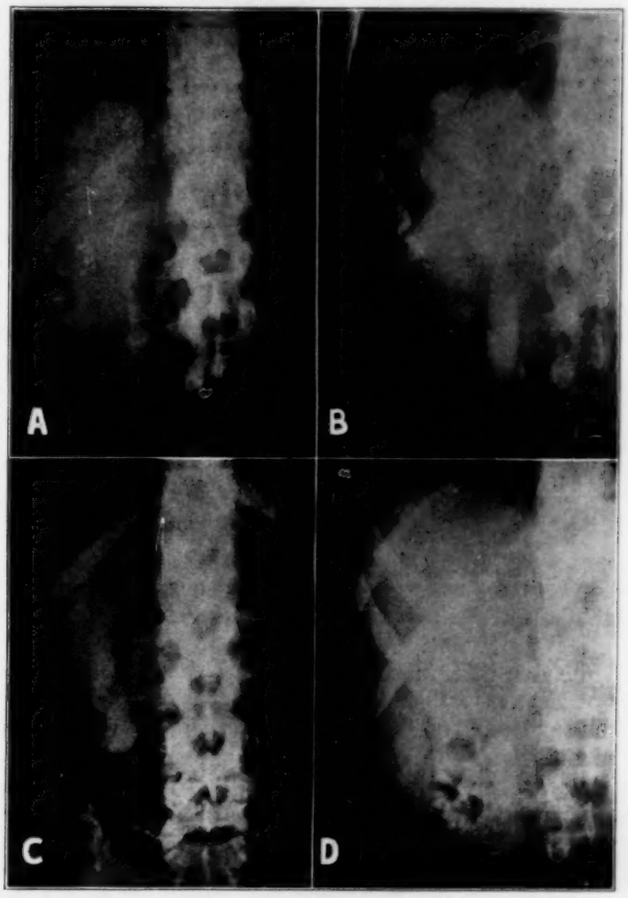

Fig. 1 (case 1).—*A* and *B*, preoperative cholecystograms, *A* taken fifteen hours after the administration of dye and *B* one hour after a fatty meal. *C* and *D*, postoperative cholecystograms, *C* taken fifteen hours after the administration of dye and *D* one hour after a fatty meal.

Titone [19] reported a series of twenty-five cases in which dyskinesia of the gallbladder was relieved by appendectomy. He presented the preappendectomy and postappendectomy cholecystograms in six instances, demonstrating a return to normal visualization and emptying of the gallbladder following the removal of the appendix. Poenaru-Caplescu [20] reported a similar case. He, however, believed that cholecystitis with-

From the Combined Medical and Surgical Biliary Tract Clinic of the New York Post-Graduate Medical School and Hospital of Columbia University.

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out stones existed prior to appendectomy. Kadrenka [21] late in 1937 reported a series of thirty-three cases of known appendicitis in which there was normal visualization of the gallbladder but typical symptoms of cholecystitis. In ten of these there was delayed evacuation

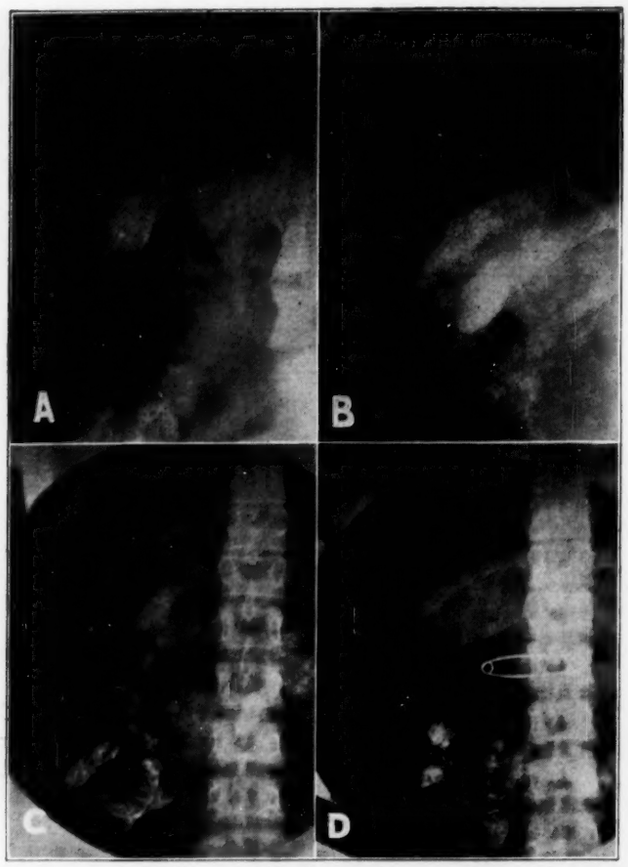

Fig. 2 (case 2).—*A* and *B*, preoperative cholecystograms, *A* taken fifteen hours after the administration of dye and *B* one hour after a fatty meal. *C* and *D*, postoperative cholecystograms, *C* taken fifteen hours after the administration of dye and *D* one hour after a fatty meal.

of the dye after a fatty meal. Relief was secured by appendectomy. There is then some evidence of a clinical syndrome of definite reflex spasm of the biliary tract secondary to appendicitis.

We are presenting three cases of dyskinesia of the gallbladder in which the removal of a diseased appendix has resulted in the relief of the dyskinesia. This is evidenced by the relief of symptoms, i. e. colic, nausea, diffuse discomfort, distention and vomiting; by a postoperative cholecystogram showing normal visualization and normal emptying of the gallbladder, and by biliary drainage showing a normal response to magnesium sulfate and olive oil.

REPORT OF CASES

CASE 1.—*History.*—A. P., aged 31, who presented himself for treatment Nov. 1, 1935, by courtesy of Dr. Bernard Marraffino of New York City, had had cramplike and nonradiating pain in the right upper quadrant for four years. For the past two months it had been of greater severity. There was never any nausea or vomiting, but occasionally belching and sour eructation occurred after meals. The symptoms were not related to any particular type of food. The pain had always begun about ten minutes after each meal and lasted for a half hour. The patient had had influenza seventeen years before but no other serious illnesses and no operations. He was married and had one child, aged 3 months, who was living and well.

21. Kadrenka, S.: Appendix: Functionally Controlled Distant Symptoms, Fortsch. a. d. Geb. d. Röntgenstrahlen **56**: 67-75 (July) 1937.

Examination.—The patient was thin and poorly developed. The only significant observations at physical examination were abdominal tenderness over the iliac colon and in the right lower quadrant, over the cecum. The iliac colon was tubelike, firm, tender and easily movable under the palpating hand. A cholecystogram showed a large hypertonic gallbladder with good concentration but a marked delay and incomplete evacuation after a fatty meal. There was no evidence of lithiasis (fig. 1 *A* and *B*). A gastrointestinal series showed the complex of duodenal irritation with marked diverticular pouching of the duodenum. There was a suggestion of a small erosion in the duodenal pouching. The likelihood of chronic appendicular thickening was observed.

The diagnosis was (1) functional disorder of the biliary tract or dyskinesia of the gallbladder, reflex in type, (2) diverticulum of the duodenum, (3) spastic colon and (4) chronic appendicitis.

Clinical Course.—Between November 1935 and November 1937 the treatment consisted of the use of (1) a modified Sippy diet, low residue, with intermediate feedings, (2) belladonna and phenobarbital, (3) alkalis and (4) olive oil given by mouth. With this regimen there was a distinct improvement in that the symptoms became less severe and the attacks of pain occurred less frequently. In view of the persistent tenderness in the right lower quadrant and over the iliac colon the patient

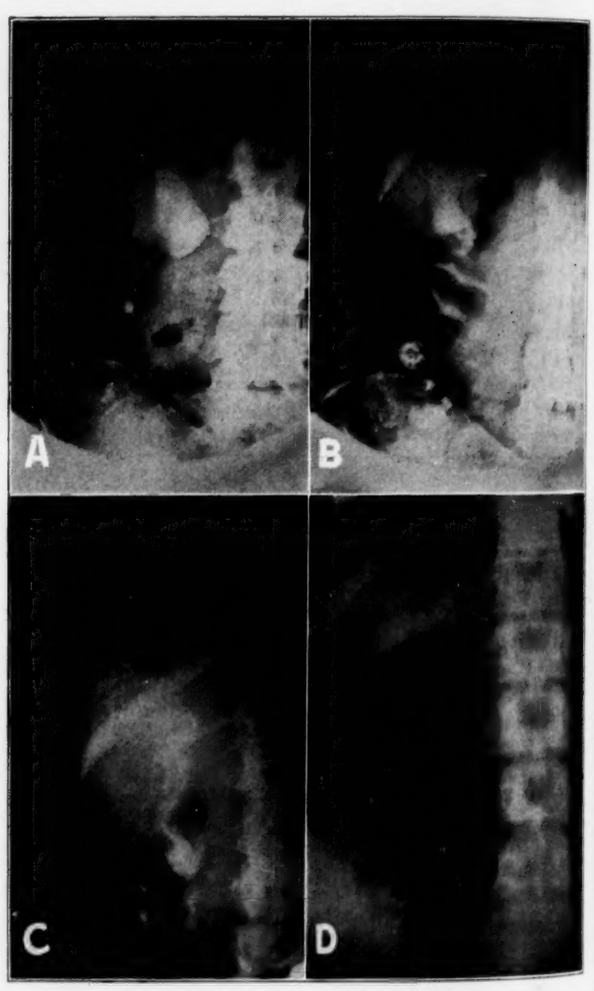

Fig. 3 (case 3).—*A* and *B*, preoperative cholecystograms, *A* taken fifteen hours after the administration of dye and *B* one hour after a fatty meal. *C* and *D*, postoperative cholecystograms, *C* taken fifteen hours after the administration of dye and *D* one hour after a fatty meal.

was advised to have his appendix removed with the hope that this was the source of the reflex disturbance.

Appendectomy was performed in November 1937. On exploration of the abdomen, the gallbladder was seen to be distended, enlarged and thin walled. There was no evidence of chronic inflammation or stones. The gallbladder emptied on moderate pressure. A diverticulum of the duodenum was found in the

second portion. The appendix was bound down and thickened but was without evidence of an acute inflammation. The pathologic diagnosis was chronic appendicitis, probably recurrent subacute attacks.

For the nine months of follow-up after appendectomy, the patient felt only slight momentary pain in the right lower quadrant on two occasions, three months and six months postoperatively. He at no time had pain in the upper part of the abdomen. Belching and sour eructation had disappeared. Moderate tenderness over the iliac part of the sigmoid flexure persisted. No medication was prescribed. A cholecystogram, made eight months postoperatively revealed normal visualization and normal emptying of the gallbladder (fig. 1 *C* and *D*). Biliary drainage was not done.

CASE 2.—*History.*—R. A., a married woman aged 34, who presented herself for treatment in the gallbladder clinic Nov. 17, 1937, had had cramplike pain throughout the upper part of the abdomen for four weeks. The pain, which radiated to the right scapula, was paroxysmal, with remissions. Nausea, vomiting and distention accompanied it. One attack of definite colic occurred during this period. No food idiosyncrasy was noted. The patient had an indefinite history of indigestion for the past seven years but no serious illnesses, no operations and a normal menstrual history. She had two children, aged 14 and 9, both of whom were living and well.

Examination.—Physical examination gave essentially negative results except to reveal slight tenderness in the right subcostal area and in the right lower quadrant. A cholecystogram taken at St. Vincent's Hospital by Dr. W. W. Maver showed an organ normal in size, with a fair concentration of dye, which emptied only about one half its contents in response to food stimuli. There was no evidence of lithiasis (fig. 2 *A* and *B*). A gastrointestinal series showed abnormal spasticity at the pylorus with delayed gastric evacuation. At twenty-four hours all the meal had passed into the colon. There was a redundant loop of proximal transverse colon which overlay the ascending colon and appeared to be more or less fixed in this position.

Duodenal drainage yielded bile containing 1,000 mg. of bile salts per hundred cubic centimeters. (A bile of Lyon),[22] after stimulation with magnesium sulfate 2,000 mg. of bile salts (light colored B bile) and after the administration of olive oil 3,000 mg. of bile salts (dark B bile). No crystals or pus cells were present. Cultures of all three specimens of duodenal bile were negative. A gastric specimen taken during fasting showed a value for free hydrochloric acid of 18.

Chemical examination of the blood disclosed 128 mg. of cholesterol and 61 cholesterol esters per hundred cubic centimeters, an icterus index of 7.8 and negative direct and indirect Van den Bergh reactions.

The diagnosis was reflex dyskinesia of the gallbladder associated with hypertonic hyperacidity of the stomach.

Clinical Course.—The patient was given alkalis, belladonna and phenobarbital. Drainage of the biliary tract was continued at intervals of three weeks. There was moderate improvement in the associated symptoms of nausea and distention. The pain continued intermittently.

April 13, 1938, the patient had increased, knifelike pain, especially in the right lower quadrant, with nausea and vomiting. Examination revealed definite McBurney point pain, rebound tenderness and right rectus spasm. An appendectomy performed April 14 revealed a suppurative process involving the appendix from its base to the tip. The gallbladder was slightly hypervascularized but free from adhesions. The foramen of Winslow and the gastroduodenal segment were normal. The pathologic diagnosis was acute phlegmonous appendicitis in an appendix showing results of previous inflammation.

During the six months of follow-up the patient had a remarkable subsidence of her gallbladder symptoms with only occasional belching and mild distress in the lower part of the abdomen. She continued the use of belladonna and a diet low in calories and fat. A cholecystogram made six months after operation showed normal visualization and normal emptying (fig. 2 *C* and *D*). Biliary drainage indicated normal function of the gallbladder, with 5,000 mg. of bile salts per hundred cubic centimeters after the administration of magnesium sulfate and 4,000 mg. after olive oil.

CASE 3.—*History.*—M. G., a married woman aged 45, who presented herself for treatment in the gallbladder clinic Dec. 1, 1937, had had colicky pain in the right upper quadrant for three years. The attacks were sudden, severe and of three or four hours' duration. They occurred once a month, accompanied by nausea, vomiting and distention. Slight intermittent pain with distention was present between attacks. The history was essentially irrelevant, there having been no previous illnesses, no operations and a normal menstrual history. The patient had five children between 15 and 26, all living and well.

Examination.—The patient was underweight but well developed and not apparently ill. Examination gave essentially negative results except to demonstrate slight tenderness in the right upper quadrant. A cholecystogram revealed a gallbladder which apparently functioned fairly well, was hypertonic and showed delay in emptying (fig. 3 *A* and *B*).

Duodenal drainage disclosed that a gastric specimen taken during fasting had a value for free hydrochloric acid of 8.5. The duodenal bile, A bile of Lyon, contained 1,500 mg. of bile salts per hundred cubic centimeters after the administration of magnesium sulfate 3,000 mg. of bile salts and after olive oil 5,000 mg. of bile salts. Occasional calcium crystals were seen. The cultures were negative.

Chemical examination of the blood revealed 209 mg. of cholesterol and 112 cholesterol esters per hundred cubic centimeters, an icterus index of 4.4 and negative direct and indirect Van den Bergh reactions.

The diagnosis was (1) mild hypertonic reflex disturbance as evidenced by a distended hypertonic gallbladder with delayed emptying and (2) possible chronic appendicitis.

Clinical Course.—The patient was given frequent feedings and also phenobarbital and belladonna. She gained weight and had a distinct decrease in symptoms until Feb. 23, 1938, when she had severe pain in the right lower quadrant for two days, with nausea and vomiting. Examination revealed pain and tenderness in the right lower quadrant with slight rigidity. She was admitted to the hospital with a diagnosis of acute appendicitis.

An appendectomy was performed immediately and disclosed that the appendix was covered with fibrinoplastic membrane. There was no evidence of gross perforation, though clear reactive fluid was present. The gallbladder was hypervascularized but without adhesions and emptied readily. A strawberry type of gallbladder without calculi was suggested. The pathologic diagnosis was acute phlegmonous appendicitis in an appendix showing results of previous inflammation (reduction of lymphoid tissue and scarring).

During the seven months following appendectomy, the patient improved remarkably. The attacks of gallbladder disturbance nearly disappeared, and their severity was eliminated. The patient still had slight nausea. A cholecystogram made four months after the appendectomy revealed a functionally competent gallbladder with normal emptying (fig. 3 *C* and *D*). Duodenal drainage indicated a normal gallbladder having a concentration of bile salts of 6,000 mg. after the administration of magnesium sulfate and 4,000 mg. after olive oil. Occasional cholesterol crystals were found. All cultures were negative.

COMMENT

A diagnosis of dyskinesia of the gallbladder was made in each case on the basis of (1) irregular occurrence of symptoms referable to the upper part of the abdomen which were primarily those of indigestion, as well as colicky pain; (2) a cholecystogram revealing no evidence of true cholecystitis (failure to concentrate the dye) or lithiasis but a delay in evacuation of the dye, and (3) the results of biliary drainage (in cases 2 and 3), which revealed evidence of spasm at the sphincter of Oddi with abnormal response to drainage stimuli.

Antispasmodics and sedatives in each instance gave some relief from acute pain but did not relieve the asso-

22. The Aldrich-Bledsoe and the Reinhold-Wilson method of bile salt determination were used in the cases presented.

ciated symptoms of nausea, vomiting, distention and belching.

Operation in each instance revealed no macroscopic evidence of cholecystitis. The appendix was acutely diseased in two instances, with evidence of long-standing chronic infection. In case 1 the appendix was chronically diseased. The relief from pain in the right upper quadrant and from the associated symptoms of distress, nausea, vomiting and distention which followed appendectomy is evidence of the probable relationship which existed between the disturbance in the appendix and the reflex spasm in the biliary tract. This clinical evidence was further substantiated in all three cases by normal results of postoperative duodenal drainage and a totally normal postoperative cholecystogram.

CONCLUSION

The reflex origin of dyskinesia of the gallbladder may be found in a chronically diseased appendix. Such a relationship seems to have been demonstrated in the three cases presented in this paper.

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AN OBSTETRIC AUDIT

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In recent years American obstetrics has been severely criticized. Certain of the criticisms have been justified. The compilation by the Children's Bureau [1] of the maternal mortality rates for the year 1929, which showed that the United States stood third from the bottom among the nations reporting to the International Health Office, was indeed discrediting; even making allowances for some differences in the methods of reporting, this country's record is bad. Two nations, Chile and Scotland, had rates that were higher than that of the United States, and Norway's rate of 3.0

TABLE 1.—*United States Maternity Mortality* *

	1937	1936	1935	1934	1933
Puerperal deaths	10,769	12,182	12,544	12,859	12,885
Rate per thousand live births	4.89	5.68	5.82	5.93	6.19
Abortions (with sepsis)	1,531	1,801	2,167	2,204	2,037
Abortions (without sepsis)	582	680	602	570	640
Ectopic pregnancy	461	486	545	571	610
Hemorrhage	1,319	1,398	1,370	1,404	1,339
Puerperal septicemia	2,113	2,705	2,902	2,808	2,729
Eclampsia	2,161	2,235	2,229	2,431	2,520
Other toxemias	556	549	497	559	535
Phlegmasia and embolus	495	567	578	561	592
Accidents	1,423	1,635	1,543	1,621	1,750

* From a United States Bureau of the Census release dated Jan. 13, 1939.

compared unfavorably with the 7.0 of the United States. In 1929 if the United States rate had been the same as Norway's there would have been 9,000 fewer maternal deaths in this country.

However, unsatisfactory as the situation was, it was not as bad as many of the articles appearing in both lay and professional journals pictured it. A statement often quoted is that 22,000 women die annually in childbirth.[2] While that was true twenty years ago, when both the birth rate and the puerperal death rate were higher, the fact is that in 1937 10,769 deaths were due to the puerperal state. Again, the statement has been made [3] that American hospitals are unsafe places in which to have a baby born. The facts will be analyzed later, but suffice it to say that the statement should not have been made to apply to all hospitals. The

TABLE 2.—*Nonobstetric Puerperal Deaths*

	New York Report	Philadelphia Report	Cleveland 1930-1937	United States 1933-1937
Puerperal deaths	2,041	717	733	61,239
Births	347,449	125,409	144,716	10,752,100
Septic abortion	262	162	134	9,740
Nonseptic abortion	95	26	25	3,074
Ectopic pregnancy	120	33	51	2,673
Nonobstetric deaths	487	221	210	15,487
Percentage of puerperal deaths	23.9	30.8	28.7	25.3
Postpartum sepsis	510	119	103	13,257
Septic abortion	262	162	134	9,740
Percentage of puerperal sepsis due to abortion	34.0	57.6	56.5	42.4

much publicized statement [4] that preventable sepsis was rampant is to say the least a flagrant misrepresentation. While there is much that can and should be done to improve American obstetrics, the situation is not as unfavorable as both the public and the profession have been led to believe.

During the years in which this barrage of criticism was descending, forces were at work which were making the criticism less and less justified. Progress in lowering the maternal death rate and in improving obstetric practice has gone steadily forward (chart 1). Since 1920, except for four years, in only one of which (1928) was the rise marked, there has been a constant fall in the maternal mortality rate. Since 1929 this fall has been accelerated, and for the year 1937 it was notable. The decrease in the rate from 5.68 in 1936 to 4.89 in 1937 was 13.9 per cent, which was greater than the decrease in the four previous years combined (6.41 in 1932). From 1929 through 1937 the fall in the maternal mortality rate was 30 per cent, and more than a third of it took place in 1937. Further, in 1938 the total number of puerperal deaths in Ohio, the only state for which I have means at present of knowing the record for 1938, fell to 425 from 490 in 1937, a decrease of 14.3 per cent.

Comparing the reduction in maternal mortality with that of the general mortality, one will see that the puerperal rate has fallen much more sharply. The decrease in the general mortality from 1929 to 1937 was 7 per cent, while the decrease in the puerperal death rate was 30 per cent for the same period.

Turning to the components of maternal mortality, one finds nine major causes the records of which are here compared for the last five years (table 1). The general decrease is gratifying but not uniform. It will be noted that there has been a decrease in the number of hemorrhagic deaths of only 1.5 per cent, while the mortality has decreased for toxemia 14.2 per cent, accidents 18.7 per cent, abortions 21.1 per cent and puerperal septicemia 23.6 per cent.

Read before the Section on Obstetrics and Gynecology of the Cleveland Academy of Medicine, April 26, 1939.

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3. De Lee, J. B., and Siedentopf, Heinz: The Maternity Ward of the General Hospital, J. A. M. A. **100**: 6 (Jan. 7) 1933.

4. de Kruif, Paul: Ladies' Home Journal, March 1932, p. 6.

TABLE 3.—*Percentage of Hospitalization and Puerperal Death Rate in Cities with a Population in 1930 of More Than 100,000 (Cities Listed in Order of Size)*

	1937 Births	1935 Hospitalization	1935 Puerperal Death Rate	1936 Hospitalization	1936 Puerperal Death Rate	1937 Hospitalization	1937 Puerperal Death Rate
Cities with More Than 5,000 Births in 1937							
New York	101,095	80.5	5.26	81.4	4.70	82.6	4.02
Chicago	49,633	71.1	4.01	75.5	4.30	77.5	3.52
Philadelphia	30,304	75.6	5.25	81.6	5.85	80.1	4.22
Detroit	27,609	52.5	6.42	58.8	5.15	68.4	3.74
Los Angeles	19,315	57.1	6.17	56.2	5.81	58.9	4.45
Cleveland	14,762	65.0	6.15	78.1	3.98	81.0	3.93
St. Louis	13,733	76.6	4.28	80.0	5.22	82.0	3.78
Baltimore	14,255	52.9	6.23	66.1	4.90	67.2	4.49
Boston	15,931	69.0	5.73	70.3	5.58	75.6	4.52
Pittsburgh	13,618	71.5	7.41	76.4	5.70	76.0	6.00
San Francisco	8,225	84.0	4.22	87.0	2.60	86.1	3.65
Milwaukee	9,991	71.5	3.32	74.4	3.12	64.5	4.21
Buffalo	9,917	69.2	5.96	69.9	6.65	72.7	4.64
Washington, D. C.	12,343	85.4	6.65	89.6	6.90	90.3	5.75
Minneapolis	8,269	89.2	6.11	88.3	5.66	92.5	3.03
New Orleans	9,557	72.4	10.39	60.0	15.05	54.1	8.49
Cincinnati	8,389	78.3	6.66	81.2	7.06	82.1	6.45
Newark, N. J.	7,633	72.9	4.59	80.0	4.29	77.7	3.14
Kansas City, Mo.	6,038	66.0	9.25	72.3	6.85	73.5	5.47
Seattle	5,419	80.5	4.49	79.1	4.33	86.0	3.32
Indianapolis	6,379	50.1	5.96	56.2	5.24	58.4	3.46
Rochester, N. Y.	5,190	82.1	5.64	83.3	6.89	82.8	3.28
Jersey City, N. J.	6,804	87.9	3.57	89.0	4.35	92.1	3.38
Louisville, Ky.	5,579	60.2	9.38	58.1	6.20	63.6	7.19
Houston, Texas	6,797	77.2	7.06	73.0	7.80	77.0	5.45
Columbus, Ohio	5,319	63.0	11.80	62.0	9.45	63.7	7.90
Denver	6,028	66.6	7.05	68.5	6.40	70.2	3.80
St. Paul	5,443	87.4	5.85	88.5	3.75	89.4	3.86
Atlanta, Ga.	6,225	84.3	7.23	85.0	6.05	82.5	6.91
Dallas, Texas	5,616	67.8	7.01	67.9	4.96	69.2	3.56
Birmingham, Ala.	5,040	62.0	9.48	76.5	13.67	64.4	8.90
Memphis, Tenn.	5,203	68.0	14.90	68.0	12.64	68.0	11.89
Providence, R. I.	5,379	85.7	5.98	88.8	3.07	89.9	4.65
San Antonio, Texas	5,934	28.2	10.12	34.6	6.65	42.0	6.58
Average		70.9	6.75	73.7	6.20	74.8	5.05
Cities with from 3,000 to 5,000 Births in 1937							
Portland, Ore.	4,806	74.5	5.03	82.9	5.03	83.5	3.74
Toledo, Ohio	4,940	60.1	8.86	66.0	6.94	68.5	6.01
Oakland, Calif.	4,931	79.1	2.21	80.1	6.20	80.4	4.26
Akron, Ohio	4,150	54.1	6.11	57.4	4.22	65.5	3.86
Omaha	4,218	69.9	6.53	73.4	6.35	81.0	5.21
Syracuse, N. Y.	3,744	79.6	4.72	84.0	4.49	86.6	5.09
Dayton, Ohio	4,205	65.0	8.31	74.3	5.02	81.3	3.80
Worcester, Mass.	3,518	83.1	6.00	81.0	4.80	85.5	6.55
Oklahoma City	3,921	67.2	6.90	67.7	9.61	78.0	6.12
Richmond, Va.	3,491	46.1	10.15	52.0	9.97	56.4	9.32
Youngstown, Ohio	3,357	42.7	9.40	54.0	3.44	60.8	6.85
Hartford, Conn.	4,028	96.1	6.25	97.8	5.02	97.5	3.73
Fort Worth, Texas	3,077	58.8	5.82	57.5	10.81	65.6	6.18
New Haven, Conn.	3,108	73.1	3.90	74.9	3.63	79.5	3.54
Flint, Mich.	3,820	57.5	7.00	63.9	5.75	71.5	4.98
Nashville, Tenn.	3,532	57.5	9.91	69.3	5.30	71.0	7.94
San Diego, Calif.	3,435	72.1	4.19	72.0	5.71	72.6	3.50
Des Moines, Iowa	3,124	65.2	6.23	46.6	3.33	65.0	5.75
Salt Lake City	3,676	76.4	6.35	82.0	6.40	87.0	4.64
Camden, N. J.	3,198	78.6	5.80	76.0	5.53	77.5	5.01
Average		67.8	6.48	70.6	5.88	75.7	5.30
Cities with from 2,000 to 3,000 Births in 1937							
Grand Rapids, Mich.	2,893	53.7	5.99	59.8	5.34	69.6	5.88
Springfield, Mass.	2,570	87.5	6.26	86.0	2.77	89.0	3.50
Bridgeport, Conn.	2,623	84.0	4.65	86.6	3.52	90.0	1.14
Scranton, Pa.	2,702	57.8	6.97	65.9	6.36	68.5	6.65
Long Beach, Calif.	2,714	56.0	2.74	51.3	3.24	58.5	2.58
Tulsa, Okla.	2,392	63.5	6.24	63.8	8.02	63.5	4.60
Paterson, N. J.	2,581	76.0	5.19	80.0	2.28	86.0	3.48
Norfolk, Va.	2,244	46.1	8.79	44.5	7.39	39.0	7.12
Jacksonville, Fla.	2,864	43.0	10.41	68.0	9.65	65.0	7.33
Albany, N. Y.	2,495	88.9	5.20	87.1	4.54	90.5	2.41
Trenton, N. J.	2,482	64.0	8.14	68.5	4.64	75.0	9.25
Kansas City, Kan.	2,270	48.8	10.29	53.6	6.34	62.0	4.85
Chattanooga, Tenn.	2,411	46.4	13.75	50.5	9.60	50.1	12.01
Erie, Pa.	2,355	66.1	8.20	67.4	5.02	70.4	5.10
Spokane, Wash.	2,408	65.4	4.35	58.5	2.69	81.5	5.81
Fort Wayne, Ind.	2,096	65.5	10.90	68.0	5.46	71.6	6.70
Elizabeth, N. J.	2,165	63.2	5.31	70.0	2.43	66.6	3.69
Cambridge, Mass.	2,123	74.5	6.26	76.1	3.82	78.8	5.17
Wichita, Kan.	2,199	53.1	4.56	63.1	3.44	65.5	4.55
Miami, Fla.	2,360	63.0	5.75	67.5	7.13	74.0	4.24
Tacoma, Wash.	2,009	87.0	6.55	82.0	7.10	89.5	4.97
Wilmington, Del.	2,497	75.1	3.08	76.5	8.35	81.5	3.60
Knoxville, Tenn.	2,215	59.4	8.81	63.1	9.98	63.1	10.40
Peoria, Ill.	2,751	80.4	8.33	87.4	4.40	76.0	5.82
Canton, Ohio	2,082	53.3	9.11	63.5	4.36	76.6	6.71
El Paso, Texas	2,618	34.8	6.63	43.2	7.27	38.9	6.90
Gary, Ind.	2,325	68.9	4.85	68.4	6.95	72.0	2.41
Average		63.9	6.94	67.4	5.63	70.8	5.44

Further analyzing these deaths, one finds that abortions and ectopic pregnancies caused a considerable proportion. These two causes, together with a small group of miscellaneous reasons for maternal death early in the pregnancy, are in no sense dependent on the obstetric management. The obstetrician does not see the patients. If they are hospitalized they do not come into the obstetric department. In fact if the hospital is a specialized maternity hospital they do not enter it at all. The general hospital, then, will have a higher puerperal death rate because it accepts this class of case. Many general hospitals not handling obstetric patients at all have a high puerperal death rate because of them. Deaths from abortions and ectopic pregnancies therefore are not a proper charge on obstetrics. There should be an additional classification, the obstetric death rate, determined from deaths attributable to the obstetric care, those occurring subsequent to the time of viability of the child, the deaths due to abortion, ectopic pregnancy and other nonobstetric conditions of early pregnancy being excluded. Deaths due to abortion

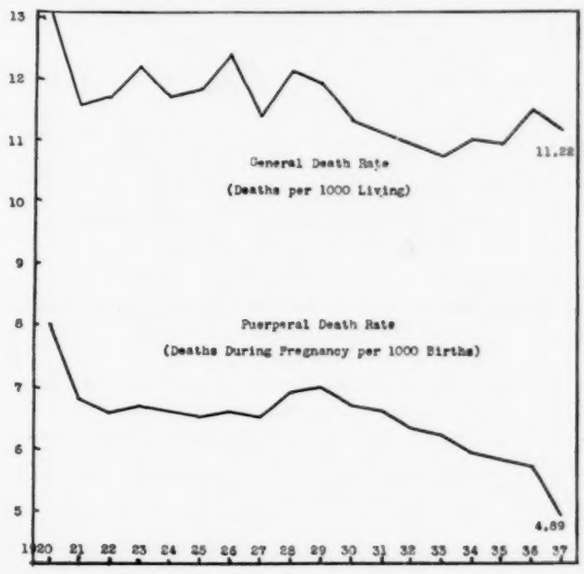

Chart 1.—General death rate and puerperal death rate, United States registration area, 1920-1937.

are a proper component of the puerperal death rate, which denotes the risk of pregnancy, but not of the obstetric death rate, which denotes the risk of delivery.

Taking the figures from three studies that have been made [5] and the census bureau figures for the last five years (table 2) and excluding the deaths from abortion and ectopic pregnancy, one finds that the obstetric death rate is somewhat less than three fourths of the puerperal death rate.

Further, since abortion is not a part of the obstetric risk, the sepsis that is incident to the abortion should not be included with the infective conditions that arise at the time of delivery. Almost half of the deaths commonly classified as due to puerperal septicemia are due to abortion. Hence figures that include deaths from this cause give the impression that sepsis causes many more obstetric deaths than it actually does. If there had been a general understanding of these facts, so much criticism would not have been leveled at obstetric infection.

5. Report of Maternal Mortality Committee of the New York Academy of Medicine, 1935. Report of the Maternal Mortality Committee of the Philadelphia County Medical Society, 1936.

Studying the puerperal deaths as they occur throughout the United States, one finds a great variability in different localities (chart 2). In 1937 the maternal mortality for the states ranged from a low of 25 per

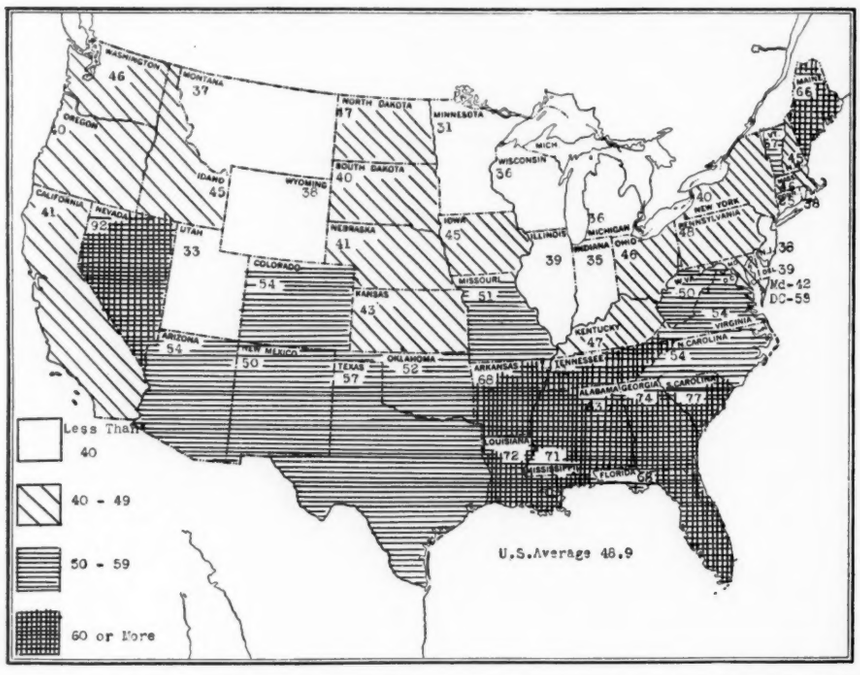

Chart 2.—Maternal mortality in the United States, 1937; puerperal deaths per 10,000 births. Source, Children's Bureau, U. S. Department of Labor.

10,000 births in Connecticut to a high of 92 in Nevada, a rate almost four times as great. Twelve of the states had a rate below 40 and ten a rate above 60.

The improvement made in the past six years is significant (chart 3). Since there may be incidental variations in any one year's rate that might make comparison unfair, the average rate for each state for 1930 and 1931 is compared with the average rate for 1936 and 1937. There was a fall of 22.3 per cent for the entire United States in this period. One fourth of the states had a drop of more than 25 per cent, while one fourth had a drop of less than 15 per cent. Some of the states with the lowest rates in 1937 did not show a great decrease because their rates had been relatively low for a considerable period, while some of the states whose rate was still high showed marked improvement.

The cities have an even greater divergence in maternal mortality. Eighty-one cities in the United States with a population of more than 100,000 had more than 2,000 births in 1937 (table 3). Studying the figures for this group of cities for the past three years, one can make some interesting deductions. Of the 243 puerperal death rates, fifty, or 20.6 per cent, are below 4 and forty-one, or 16.9 per cent, are above 8 deaths per thousand live births. Eleven of the cities have rates below 4 more than once, and nine have rates above 8 more than once. In other words, about one seventh of the cities have a very creditable record and one ninth have a poor one. Comparing the percentage of hospitalization with the puerperal death rates, one sees that in almost every instance in which the rate is good the rate for hospitalization is high, averaging 76.7 per cent, while in the instances in which there is a poor puerperal death rate the percentage of hospitalization, except in a few cases, is low, averaging 60.2. In the cities having a large number of births the percentage of hospitalization tends to be either higher and the puerperal death rates lower and the experience from year to year has a less wide variation.

No specific study has been made of the improvement in the city rates because of the great variations that occur in some of them, at times because of the relatively small number of cases in any year and again because of the markedly different conditions that exist among the cities. Particularly deviating from the normal are those cities that have large surrounding areas from which patients are drawn to the metropolitan hospitals. In some cities, Columbus, Ohio, for example, a high percentage of the puerperal deaths occur in nonresident patients. In other cities some of the hospitals are in the suburbs and the city's rate is thus improved. A case in point is Milwaukee, with the city-

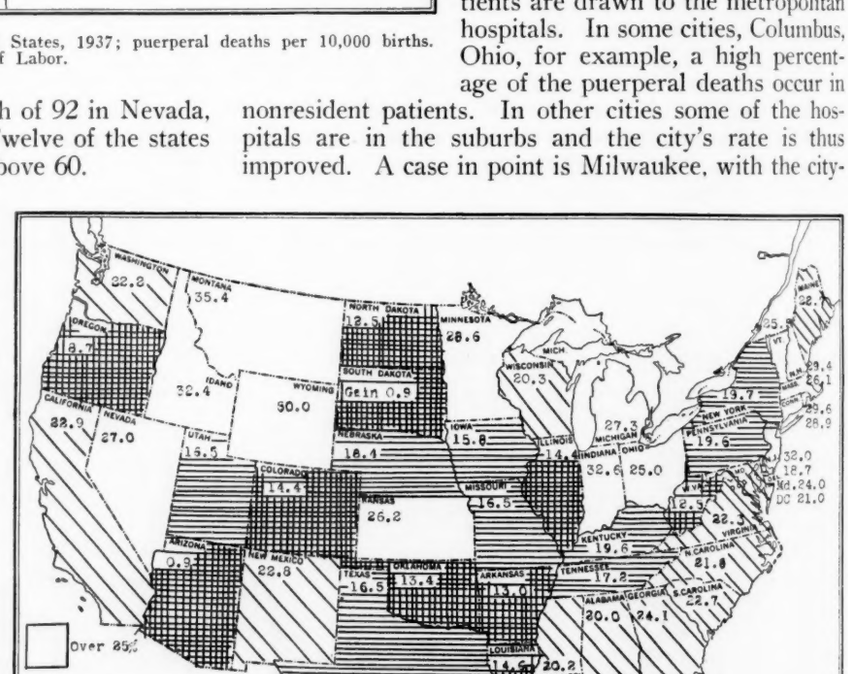

Chart 3.—Percentage of decrease in maternal mortality, 1930-1931 to 1936-1937.

county hospital in Wauwatosa outside the city registration area. In other cities, such as Boston, many patients receiving the best obstetric care live outside the city area but are delivered in the city hospitals. These and other factors affect the city rates in varying degrees and make comparisons confusing and unfair.

The contribution of cities to the puerperal death rate as compared with that of rural areas is worthy of note (chart 4). The puerperal mortality of the cities varies from 10 to 20 deaths per 10,000 births in excess of that of rural areas. The contribution of each group to the total is about equal, 5,876 deaths in cities to 4,893 in rural areas in 1937. However, it will be noted that in 1920 the difference was less than it was in subsequent years, and if the chart had been carried into previous

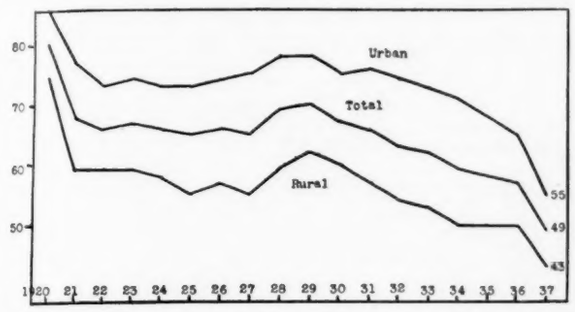

Chart 4.—Puerperal death rate in cities with a population of more than 10,000 as compared with the total rate and the rural rate; source, Bureau of the Census, March 29, 1939, vol. 7, No. 29, p. 108.

years this difference would have diminished even more. This increase in the preponderance of urban puerperal deaths can be attributed to the increase in the prestige of the urban hospital during that period and to the fact that patients in a serious condition were taken to the city hospitals in a final effort to save life. Again, in 1937 this divergence between the urban and rural rates lessened, and this reduction can be explained by the improvement that has recently occurred in the puerperal rates of hospitals.

This understanding of the reason for the increase in the number of puerperal deaths in cities, that is, the influx of nonresident patients who are taken to the city hospitals on account of the development of some serious condition that makes care in their home environment inadequate, points the way to the explanation of another comparison that has long been confusing. The hospital puerperal death rate is larger than the home rate and many have unthinkingly criticized the hospital because of this fact. In the Cleveland study of puerperal deaths, 84 per cent of the women who died in hospitals were found to have had a known pathologic condition on entrance. It has become increasingly true that if serious complications develop during labor at home the patient is taken to the hospital. A great number who would have died at home are saved by the efficient care available in the hospital. However, the hospital death rate is and will continue to be augmented as long as women are rushed to the hospital as a last resort. As more and more women go to well managed hospitals for delivery the ideal will be approached and only the unavoidable deaths will occur.

Returning to the consideration of the obstetric situation in the states, one finds three factors that contribute to the character of the obstetric care which can be accurately evaluated. These are, in the order of increasing importance, the percentage of nonwhite births, the percentage of care by graduate physicians and the percentage of hospitalization of obstetric patients.

The nonwhite births (chart 5) are largely in the extensive Negro population in the South and the smaller Indian population in the Western states, with a sprinkling from the Asiatic population in the Pacific states. One fourth of the states have less than 2 per cent and one fourth more than 10 per cent of nonwhite births. This factor certainly has a bearing on the high obstetric rates in the South; however, since nonwhite births comprise only one eighth of the total births and since for one half of the United States less than one birth in twenty is not white, this factor has no great effect on the general puerperal rate (chart 6). Not only does the general curve remain close to the curve for the white race, but severe fluctuations in the "other race" curve are not reflected in the general curve.

The percentage of women delivered by graduates in medicine (chart 7) is somewhat more significant. It demonstrates that the midwife problem and that of the mother who has no attendant are not potent factors in the puerperal death rate in the greater part of the country. But it will be noted that in some states in the South midwives deliver many of the women, and this factor probably has considerable significance in the poor record of these states. However, these are the states in which all the detrimental factors accumulate. In one fourth of the states all but 0.5 per cent of women in labor are under the care of a graduate in medicine; in another fourth all but 2 per cent are thus attended. Then, at the other extreme, there are ten states in

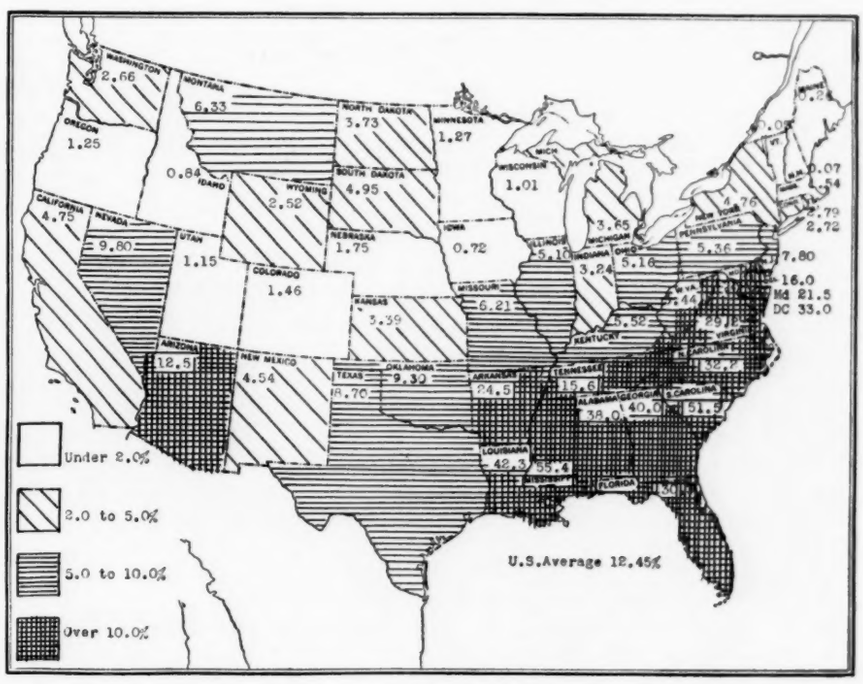

Chart 5.—Percentage of nonwhite births, 1937.

which one fourth of the women do not have medical care.

The third measurable factor is of greater significance (chart 8). The percentage of births that occur in hospitals comes closest to indicating the position a locality will have in its maternal mortality standing. One fourth

of the states have more than 60 per cent of their births in hospitals, while the last fourth have less than 25 per cent in hospitals. The average for the United States in 1937 was 44.8 per cent. Comparing the percentage of hospitalization in the various states for 1937 (chart 8)

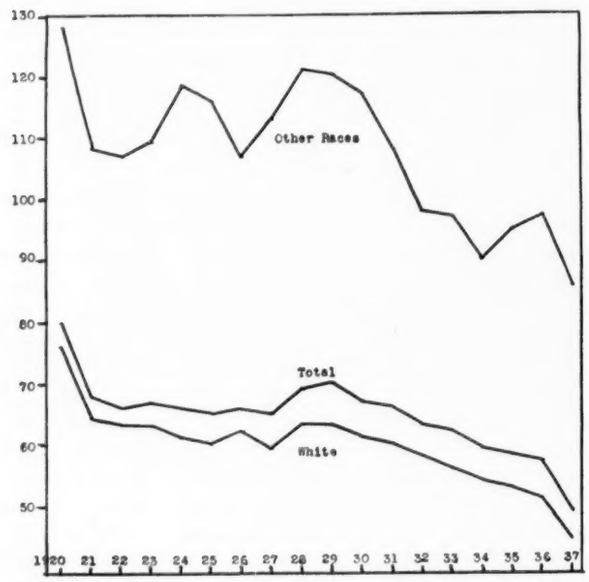

Chart 6.—The trend of maternal mortality by race, 1920-1937, puerperal deaths per 10,000 births; source, Bureau of the Census, March 29, 1939, vol. 7, No. 29, p. 112.

with the maternal mortality rates in the same states for the same year (chart 2), one makes the striking discovery that twenty-two states fall in the same category on the two charts and that only three states show any marked deviation. This extent of parallelism in the two charts is the strongest possible argument in establishing the fact that the extent of hospitalization determines the incidence of maternal mortality.

The importance of the hospital as the major factor in the control of maternal mortality is further evidenced by the great increase that has occurred in the hospitalization of the obstetric patient. Unfortunately, accurate statistics showing this trend are available only for the last few years, since the annual publication of the survey of hospitals by the American Medical Association (chart 9). Obstetric hospitals may be divided into five groups according to the number of patients handled: (1) those that have more than 100 births a month, or more than 1,200 a year; (2) those that have more than fifty births a month, or more than 600 but less than 1,200 a year; (3) those that have more than twenty-five births a month, or more than 300 but less than 600 a year; (4) those that have more than twelve and one-half births a month, or more than 150 but less than 300 a year, and (5) those that have less than twelve and one-half births a month, or less than 150 a year. The figure of twelve and one-half births a month was chosen as the minimum because practical isolation of the obstetric department is impossible with less than an average occupancy of four patients. In constructing chart 9 the number of births in the next smallest group was superimposed on the number of births in the smallest group. In 1938, for example, there were 135,000 births in hospitals having less than twelve and one-half births a month and 154,000 births in the next group, having more than twelve and one-half births a month; hence the total charted was 289,000. This process was repeated for each succeeding group, so that the top line gives the total births for all hospitals for each of the four years considered.

TABLE 4.—*Puerperal Mortality in Ohio Hospitals*

		No. of Hospitals	Births	Puerperal Deaths	Puerperal Rate
Hospitals approved					
For residencies.....	1937	17	19,169	119	6.22
	1938	22	25,401	109	4.29
For internships only.....	1937	22	14,777	98	6.65
	1938	21	14,374	68	4.74
Hospitals not approved for graduate training					
Having more than 150 births a year	1937	40	12,898	119	9.23
	1938	45	14,380	107	7.45
Having less than 150 births a year	1937	66	4,304	78	18.10
	1938	73	3,886	73	18.80

Studying these figures, one sees some interesting trends: 1. The total number of births in hospitals has increased 321,000, or 46.5 per cent, in four years. This tendency has been accelerated in the past two years, the increase having been 101,000, or 14.5 per cent, in 1937 and 91,000, or 13.1 per cent, in 1938. 2. The increase has been almost entirely in the three groups of larger hospitals. In fact, in the group having between fifty and 100 births a month the number has more than doubled in the four years, having increased from 134,000 in 1934 to 290,000 in 1938. On the other hand, hospitals having less than twelve and one-half births a month had fewer births in 1938 than they had in 1934, 135,000 as compared with 143,000.

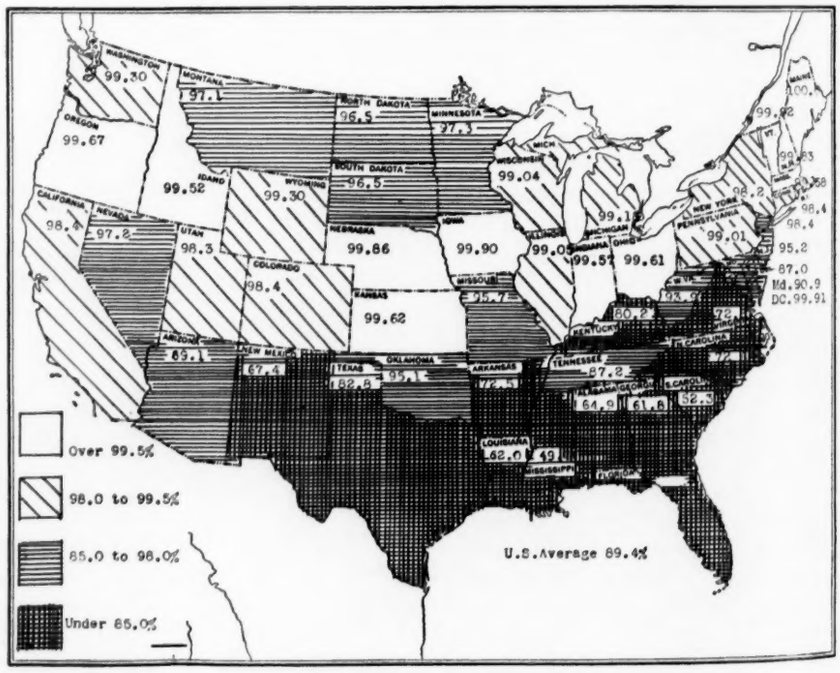

Chart 7.—Percentage of women delivered by a physician, 1937.

In studying the number of hospitals in each group according to the number of births, one observes at once that the total number of hospitals has made but slight increase in the four years, rising from 3,892 to 4,022,

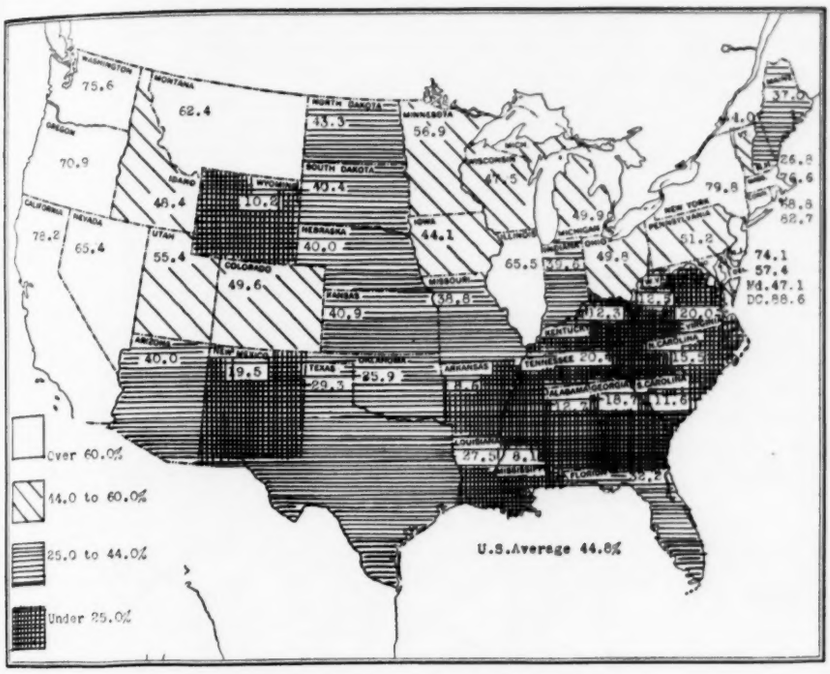

Chart 8.—Percentage of births in hospitals, 1937.

or 4.1 per cent. However, the significant thing is the increase in hospitals handling a large number of obstetric patients. Hospitals handling more than 100 births a month increased from sixty-four to 103, or 61.0 per cent, and hospitals handling from fifty to 100 births a month more than doubled, increasing from 168 to 355, percentage increases that closely approximate the increase in births for the same groups for the same period. At the other end of the scale, hospitals caring for less than twelve and one-half births a month decreased from 2,632 to 2,252, or 14.4 per cent, in the four years. The implication of these figures is that hospitals that were small, obstetrically speaking, in 1934 rapidly expanded in these four years. The enormous increase in the hospitalization of the obstetric patient is, it goes without saying, the fundamental fact from which all these changes spring. In an increasing number of hospitals the care of obstetric patients is a growing proportion of the work.

Perhaps in no small measure responsible for this increase has been the growing sense of responsibility felt by hospitals for the character of the work being done within their walls. In many localities the hospitals have used various methods to supervise the obstetric department. The "standards" adopted by the Hospital Obstetric Society of Ohio, the recommendations of the Philadelphia County Medical Society and the regulations of the Chicago Board of Health and the Maternal Welfare Committee of the Chicago Gynecological Society are but a few of the efforts to raise the standards of obstetric practice and to increase the safeguards surrounding each patient. More recently the obstetric standards set up by the American Hospital Association [6] and the pronouncement last year by the American College of Surgeons,[7] including the provision that the chief of the obstetric division of a hospital must have supervision over all patients, both staff and private, in the institution, have added force to the movement. Most recently the United States Bureau of Maternal and Child Health [1] went on record as recommending "that the enforcement of the obstetric code of each hospital must be under the supervision" of the obstetric director of that hospital and that "each hospital shall secure the signature of each physician having the privilege of obstetric practice in that hospital to" a pledge committing that physician to consultation whenever, in the opinion of the hospital authorities, complications have arisen.

Such provisions have definitely drawn the line between a hospital which is obstetrically safe and one that is a hazardous place for the expectant mother. In summary, there are two types of safeguard that are fundamental:

1. That the hospital maintain proper obstetric regulations, especially isolation of the department, as outlined by the American Hospital Association.

2. That the hospital have a proper staff organization, including a chief, with power to enforce consultation for all questionable conditions.

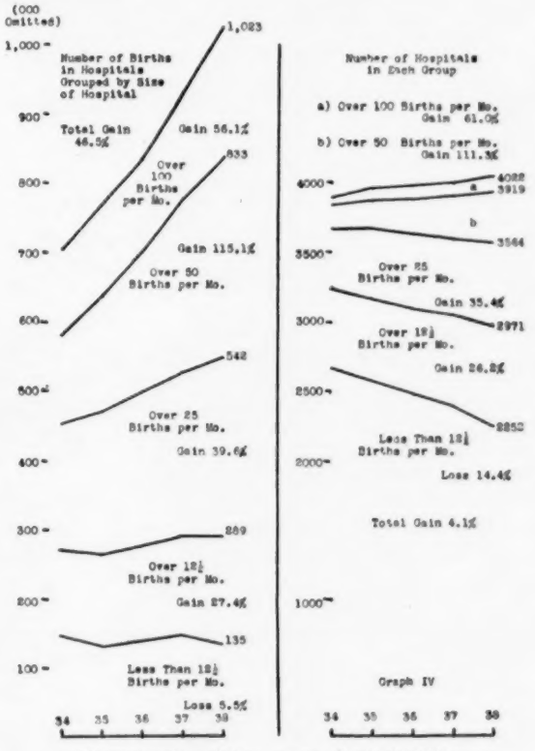

Chart 9.—Cumulative curves for 1934-1938.

A striking example of the value of these criteria is shown by a survey of Ohio hospitals for the years 1937 and 1938 (table 4). The facts stand out so clearly that

6. Manual on Obstetrical Practice in Hospitals, Chicago, American Hospital Association.

7. MacEachern, M. T.: Program of American College of Surgeons for Maternal Care in General Hospitals, Am. J. Obst. & Gynec. **35**: 535 (March) 1938.

it seems almost unnecessary to comment on them. Approved hospitals are the safest possible places for delivery, and as the regulations discussed become more effective these hospitals are becoming safer. Unapproved hospitals do not have a commendable record, and hospitals that have too small an occupancy to maintain isolation are a distinct menace. The figures point to the conclusion that unless a hospital can meet the approved standards for obstetric care it should not take obstetric patients. The group of small hospitals, as previously shown, is rapidly diminishing the country over, and reports such as the Ohio survey only emphasize the desirability of such an elimination. Only hospitals that can meet the standards of the American Hospital Association and the American College of Surgeons are proper institutions for the obstetric patient.

CONCLUSIONS

1. United States obstetrics has been making decided and accelerated strides in the reduction of maternal mortality.
2. The hospitalization of obstetric patients has markedly increased.
3. Supervision by the hospital of the character of the obstetrics practiced within its walls and the enforcement of early consultation in the case of abnormal labor has become recognized as essential.
4. As the births of the United States increasingly occur in well organized hospitals and come increasingly under the supervision of trained obstetricians, maternal mortality and morbidity will continue to improve.
5. If obstetric conditions were as favorable over the entire United States as are those existing today in a quarter of the country, there would be an annual saving of 2,500 lives.

9400 Euclid Avenue.

Clinical Notes, Suggestions and New Instruments

ACTINOMYCOSIS OF THE GALLBLADDER

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Isolated actinomycosis of the gallbladder has been reported in only a few instances. Mayo-Robinson [1] reported the first case in the literature in 1905. His case is of great interest in that it was followed up for four years, during which time there was no recurrence of symptoms. Since then Good [2] has mentioned two cases in which the primary lesion was found both in the gallbladder and in the appendix.

In view of the rarity of this lesion, we thought it worth while to report this case.

REPORT OF CASE

History.—Mrs. A. H., a middle-aged white woman, was admitted to the Cook County Hospital May 30, 1938, with a tentative diagnosis of acute cholecystitis. On questioning, the patient stated that for the last twenty years she had had attacks of pain in the upper part of the abdomen which were attributed to gallbladder trouble. The attack prior to the one for which she was admitted occurred about two years before. It was characterized by sharp, steady pains, which were felt in the upper part of the abdomen and radiated to the back. These pains often started after the ingestion of fatty or fried foods. Between attacks the patient was quite free from pain, although she would belch frequently.

The present attack began Friday May 27, following a meal of ham and cabbage. At first the pain was dull and steady, letting up somewhat the following morning after a number of anodyne tablets had been taken. The next day the pain in the right upper quadrant became very sharp and steady. It continued until the following morning, when the patient entered the hospital for treatment.

On physical examination the patient was well developed and was suffering severe pain in the abdomen, appearing acutely ill. The pulse was 118 and regular. Respirations were 28 a minute and the blood pressure was 140 systolic, 75 diastolic. The temperature was 101.8 F. The pupils were contracted and reacted to light and in accommodation. The lips were pale and the teeth were in poor condition. The chest was resonant throughout, and expansion was equal on the two sides. The breath sounds were clear. The heart was of normal size and no murmurs were heard. The mammae were normal. The abdomen was obese with distinct striae. Marked tenderness and rigidity were noted over the right upper quadrant but was less marked over the rest of the abdomen. Rebound tenderness was elicted over the entire abdomen. The liver was two finger-breadths below the right costal arch. The peristaltic rate was 30 a minute. Vaginal examination was essentially negative except for a lacerated cervix and a firm retroflexed uterus. The uterine adnexa were normal. Rectal examination was negative. In view of these clinical observations a diagnosis of acute cholecystitis and cholelithiasis, probably associated with an old hepatitis, was made.

Fig. 1.—Gallbladder showing the grayish white membrane adherent to the mucous membrane in which the actinomycetes were found. This is particularly marked in the fundus of the gallbladder.

Laboratory examinations revealed hemoglobin 80 per cent, erythrocytes 4,360,000 and leukocytes 22,750. The Kahn reaction of the blood was negative. Examination of the stool revealed blood 2 plus on one occasion. The urine showed albumin 1 plus and a few polymorphonuclears. A Graham Cole visualization of the gallbladder was negative.

In view of the persistent pain and the failure to respond to medical treatment, the patient was transferred to the surgical department for removal of the gallbladder.

The patient was operated on by Drs. Sullivan and Francona June 10. A Judd incision was made to expose the gallbladder. An impacted stone was dislodged from the cystic duct through an incision of that duct. The cystic duct and artery were then separately ligated and the gallbladder was removed.

From the Departments of Surgery and Surgical Pathology, Cook County Hospital.

1. Mayo-Robinson, A. W.: Actinomycosis of the Gallbladder, Tr. M. & Chir. Soc., London **88**: 225, 1905.
2. Good, L. P.: Actinomycosis of the Abdomen, Arch. Surg. **22**: 307 (Feb.) 1930; Actinomycosis of the Thorax, ibid. **21**: 786 (Nov.) 1930.

Pathologic Examination.—The specimen consisted of a gallbladder, previously opened, which measured 8 cm. in length and 7 cm. in circumference. The serosa was injected, a purplish gray, and the wall was thickened up to 8 mm. The mucosa was a purplish red and in places was covered by fairly large firmly adherent gray-white plaques (fig. 1). The lumen was filled with numerous faceted stones measuring up to 8 mm. in diameter. A section was taken through the entire thickness of the wall, including the gray-white plaque adherent to the mucosa.

Fig. 2.—Section showing numerous gram-positive actinomycetes surrounded by polymorphonuclear leukocytes. Gram-Weigert stain; reduced from a photomicrograph with a magnification of 72 diameters.

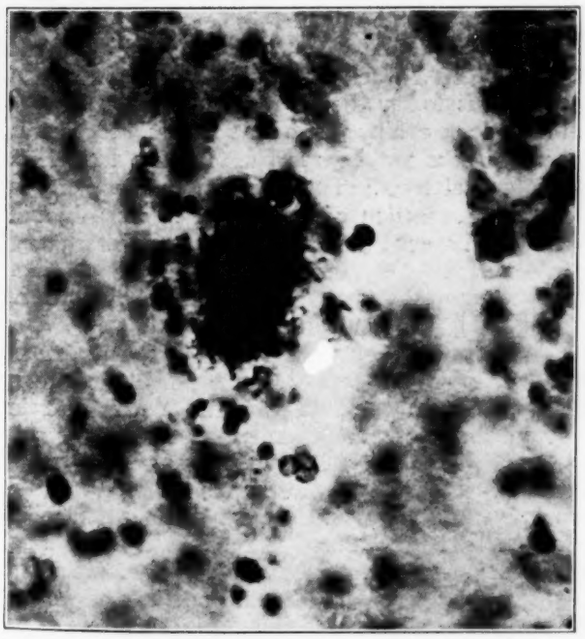

Fig. 3.—Section showing the characteristic colony of the actinomycetes in the mucous membrane of the gallbladder. Gram-Weigert stain; × 1,000.

A section of the gallbladder stained with hemalum and eosin revealed a markedly thickened wall infiltrated with many lymphocytes and large mononuclear cells, some of which were multinucleated. The arterioles and capillaries were dilated and the walls of the former were moderately thickened. In places the endothelium showed a moderate hypertrophy and hyperplasia. The mucous membrane was replaced by a necrotic membrane heavily infiltrated with many polymorphonuclear leukocytes, large mononuclear cells and a few lymphocytes. In one portion of the membrane, near the surface, were small, irregular granular, bluish staining areas surrounded by a single row of polymorphonuclear leukocytes. On staining a section with Gram-Weigert stain the granular areas were found to be composed of a filamentous gram-positive structure (fig. 2). The filaments were granular with slight clubbing of the free ends (fig. 3). In addition, single filaments were seen surrounded by polymorphonuclear leukocytes and large mononuclear cells (fig. 4).

COMMENT

The diagnosis of the actinomycotic infection of the gallbladder was not made grossly, and therefore we were unable to cultivate the ray fungus. However, the microscopic study showed distinct ray-shaped clusters and more loosely arranged branched slender mycelia, which may be classified as Cohnistreptothrix israeli because of the typical radiating colonies found in the necrotic membrane. The actinomycotic infection of the gallbladder in this case was most likely due to a retrograde extension of the infection from the gastrointestinal tract into the gallbladder. This is substantiated by the fact that the ray fungus was found only on the surface of the mucosa and in no place were we able to find the actinomycosis in the wall of the gallbladder or in the lumen of the blood vessels.

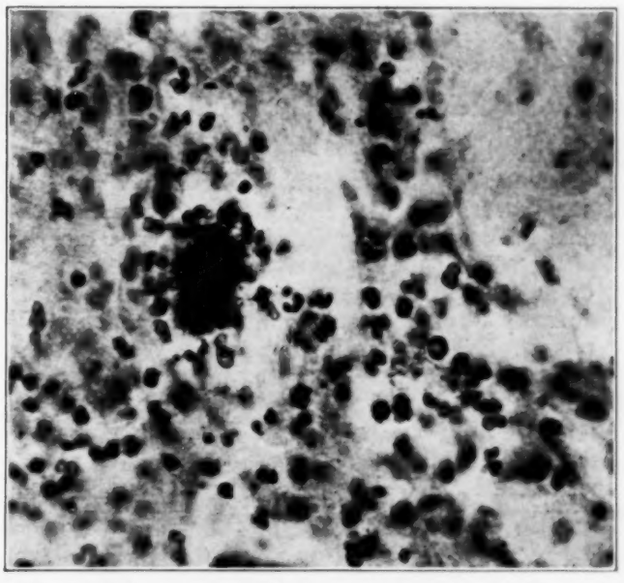

Fig. 4.—Section of the gallbladder mucosa showing single mycelial threads of the actinomycetes surrounded by mononuclear cells and polymorphonuclear leukocytes. In addition is seen a small ray fungous colony in poor focus. Gram-Weigert stain; reduced from a photomicrograph with a magnification of 1,000 diameters.

The patient, seen seven months after the cholecystectomy, stated that she had been completely alleviated of pain and the symptoms experienced prior to her operation and that the wound had completely healed. Mayo-Robinson in his report states that the patient was well for four years following a cholecystostomy.

As to the primary focus of infection in our case, several possibilities must be considered: First, the carious teeth; Klinger [3] states that the organism is an obligatory parasite, i. e. a permanent inhabitant of the mouth. Shapiro,[4] quoting Sanford and Magath, and Zinninger, stated that the primary source of infection in 60 per cent of the cases of actinomycosis has been carious teeth. The lungs too may be a primary source of infection, as found in 14 per cent of the cases of actinomycosis. The intestine is found to be a primary source in 18 per cent of the cases.

Our patient had poor teeth, and it is possible that the primary infection may have been in the teeth or in the duodenum. No other actinomycotic lesions were found in the patient.

3. Klinger, in Lehmann, K. B., and Neumann, R. O.: Bacteriology, Especially Determinative Bacteriology, ed. 7, English translation, edited by R. S. Breed, New York, G. E. Stechert & Company **2**: 776, 1931.
4. Shapiro, P. F.: Generalized Actinomycosis (Pyemic Form), Arch. Path. **12**: 397 (Sept.) 1931.

SUMMARY

In a case of actinomycosis of the gallbladder in a middle-aged white woman, periodic attacks of gallbladder colic had been occurring for the past twenty years. Microscopic examination of the gallbladder revealed colonies of the organisms characteristic of the ray fungus. Following removal of the gallbladder the patient improved and did not experience the subjective symptoms existing prior to the operation. The infection, we believe, was due to a retrograde spread from the intestinal tract, since it was limited to the mucous membrane of the gallbladder.

1825 West Harrison Street.

Special Article

CONFERENCES ON THERAPY

THE USE OF ANTHELMINTICS

NOTE.—*These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital, with collaboration of other departments. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors.*

DR. HARRY GOLD: The conference this morning is on the subject of anthelmintics and the treatment of intestinal parasites. There are several varieties of intestinal worms and many anthelmintic agents. Chapters in textbooks on this subject, if they affect you as they do me, will often leave you with no clear idea what anthelmintics are most effective in the different forms of infestations. Evidence on these matters is very difficult to secure, and the impression is difficult to escape that the shift of interest from one anthelmintic agent to another is sometimes a matter of fashion. It is hoped that the discussion this morning will help to clarify some of the problems. Dr. Travell will begin the pharmacologic discussion.

DR. JANET TRAVELL: This is a list of the helminths which most commonly infest the human intestine, and which one may be called on to treat:

Cestodes or flatworms: 1. Tapeworms: *(a)* Taenia saginata (beef); *(b)* Taenia solium (pork); *(c)* Diphyllobothrium latum (fish).

Nematodes or roundworms: 2. Hookworms (Necator and Ancylostoma). 3. Roundworm (Ascaris). 4. Pinworm (Oxyuris). 5. Whipworm (Trichuris).

I have also listed some of the anthelmintic drugs which have come into, and in some instances have gone out of, fashion:

Thymol.
Beta-naphthol.
Hexylresorcinol.
Other alkyl-hydroxyphenols.
Carbon tetrachloride.
Tetrachlorethylene.
Oil of chenopodium.
Ascaridole (active principle of oil of chenopodium).
Mixtures of oil of chenopodium or ascaridole with either carbon tetrachloride or tetrachlorethylene.
Santonin.
Oleoresin of aspidium, or extract of male fern.
Pelletierine.
Cusso.
Sap of the fig tree.
Solutions of various astringents and antiseptics for rectal instillation.

Why is there such a long list of drugs and what are the reasons for the confusion existing, as Dr. Gold has indicated, as to which is the most effective agent in the treatment of infestation by any one of these parasites?

First, there is difficulty in obtaining good criteria for evaluating effectiveness. One might think that it would be a relatively simple matter to administer a series of these vermifuges to comparable groups of patients and to determine what percentage of each group was cured, which would certainly afford a satisfactory basis for comparison. As a matter of fact, however, this method can be applied practically only to tapeworm infestations. Sanground recently studied several anthelmintics by this technic and found that in tapeworm infestations 4 cc. of carbon tetrachloride cures at least 75 per cent of the patients treated, 4 cc. of tetrachlorethylene only 35 per cent, and hexylresorcinol in total doses of from 1 to 6 Gm. only 29 per cent.

One source of error in determining the percentage of patients cured is that reinfection after treatment may occur, and this possibility makes it difficult to establish the fact as to whether a cure was or was not obtained. In the case of the tapeworms, man usually harbors only the adult form; and the intermediate host, that is, the cow, hog or fish, harbors the larvae. Reinfection, therefore, is usually easily prevented by merely instructing the patient in the importance of thoroughly cooking meat and fish and probably does not introduce any serious error in the evaluation of the results obtained in this infestation. In the case of the other parasites, however, no intermediate host is necessary. The larvae of the hookworm and Ascaris must gain access to the soil for certain stages of development, and reinfection with the larvae subsequently takes place either by penetration through the skin in the case of hookworm, or by introduction into the mouth in the case of both of these. It is therefore difficult to control the factors leading to reinfection by these two parasites. As for the pinworm, the entire life cycle takes place within a single human individual. The female migrates to the region about the anus to lay the eggs, which are then introduced into the mouth by way of the fingers. It requires only a few weeks for these larvae to attain adult form in the intestinal tract. Therefore, in the case of this parasite the prevention of reinfection is very difficult and presents a special therapeutic problem necessitating particular attention to rectal hygiene. The whipworm also has its complete life cycle in one individual and is extremely resistant to treatment.

However, the chief obstacle to using the cure rate as a criterion of effectiveness seems to be that a cure is so rarely obtained by safe doses of the anthelmintics in the case of the major infestations, that is, Ascaris and hookworm, which involve large numbers of the population and which should therefore offer the most suitable material for investigation. Hence the percentage of worms expelled has been used as the basis for comparing the different forms of treatment. In order to obtain this percentage, one must know both the number of worms expelled and the number remaining in the intestine after treatment. The former figure may be obtained fairly accurately by direct counts, although this is a laborious procedure and does not take into account those worms which may disintegrate before expulsion, and may not include those the expulsion of which may be delayed for as long as ten days. The latter figure, in the case of human beings, is of course based on estimates. These estimates are obtained either by various technics for the counting of ova continuing in the feces after treatment

or by counting the number of worms expelled after a second or "test" treatment given at a fixed interval after the first. Both the counting of worms and the counting of eggs gives only an approximate idea of the number of worms remaining in the intestine, but in addition some anthelmintics depress directly the egg-laying capacity of the parasite without killing it, so that judged by the egg-counting method, the patient may seem to be cured but subsequently the worms recover and ova reappear. It then becomes very difficult to decide whether reinfection has taken place and what percentage of the worms was removed by the treatment. Nevertheless the egg-counting method seems to be the best one available for estimating clinical efficiency. Hall has developed a direct method for evaluating the action of these drugs in experimental animals: he counts the worms expelled after treatment, then kills the animal and counts the worms that remain in the intestinal tract. The in vitro method of testing is of course less expensive and permits rapid orientation with respect to a long series of compounds. The most satisfactory test object seems to be the pig ascaris, which was first extensively used by Lamson.

In the choice of a vermifuge we are concerned not merely with the question of which one is the most effective but also with the question of which one is the safest. Let us consider first the toxic effects of one of the more important anthelmintics, carbon tetrachloride.

Carbon tetrachloride has been the most popular drug in the treatment of hookworm since it was introduced in 1922. I think Dr. Smillie, who is here today, was the first to administer carbon tetrachloride to patients, and he was the first to call attention to its toxic effects on the liver and kidneys in a report published soon after its introduction as an anthelmintic, at a time when the earlier clinical reports were exceedingly optimistic.

It is important to realize that occasionally a single ordinary therapeutic dose of this drug may prove fatal to the patient. The dose of carbon tetrachloride is now stated as from 3 to 4 cc. At the outset of its use the doses of carbon tetrachloride commonly prescribed were much larger, from 6 to 15 cc., and doses up to 40 cc. were survived. Leach reported 35,000 cases of hookworm treated with doses of from 6 to 12.5 cc. without serious poisoning, yet deaths have occurred in adults after a single dose of from 1.5 to 3 cc., and in children after less than 1 cc. At the present time the risks of poisoning with carbon tetrachloride are much less than they were ten or fifteen years ago because of the large amount of experimental work which has been done on this drug, so that we are now better informed as to how to use it, both with regard to the precautions to be observed in prescribing it and also with regard to treatment, should poisoning unfortunately occur.

Among the factors which may contribute to a fatal outcome after therapeutic doses of carbon tetrachloride, I will discuss first low calcium reserves. Dogs maintained on a low calcium diet die after very much smaller doses of carbon tetrachloride than when maintained on a high calcium diet. The mechanism of the antagonism between calcium and carbon tetrachloride is not clear, but it has been shown in dogs that the administration of calcium prevents and relieves the symptoms of poisoning and also the signs of disturbed carbohydrate metabolism, causing a restoration of the normal blood sugar level and a lowering of the accumulated blood lactic acid. Calcium does not prevent the rise in blood guanidine, which is seen in carbon tetrachloride poisoning, but is antagonistic to the toxic effects of guanidine. Calcium has no influence on the pathologic changes in the liver produced by carbon tetrachloride, the damage being about the same whether the animal is given calcium and survives or whether it is not given calcium and dies. It seems that calcium administration merely tides the patient over until regeneration of liver cells can take place, which is fairly rapid and complete. In carbon tetrachloride poisoning the total blood calcium is not materially lowered, but it is believed that there may be a reduction in ionized blood calcium. At any rate calcium is a very effective antidote.

The amount of calcium required for the treatment of carbon tetrachloride poisoning in man is not known exactly. However, when dogs maintained on a low calcium diet are given a fatal dose of carbon tetrachloride, the dose of calcium which has secured survival would be for a man, on an equivalent weight basis, about 1 Gm. of calcium a day by vein, or about 100 cc. of a 10 per cent solution of calcium gluconate, together with 5 or 6 Gm. of calcium a day by mouth. For intravenous injection the calcium salt may be conveniently added to a larger volume of dextrose solution, thus assuring that it is injected very slowly. The oral administration of calcium may be difficult because of persistent vomiting, and absorption by this route is unreliable.

The habitual consumption of alcohol is another important factor, even when no alcohol is consumed with the drug. Alcohol given simultaneously with carbon tetrachloride increases its absorption and toxicity, but I am speaking now of the habitual consumption of alcohol rather than the simultaneous administration of the two drugs. Both alcohol and carbon tetrachloride are known to injure the liver. In addition, it has been shown by Rosenthal in dogs that a small oral dose of alcohol, which of itself causes no demonstrable liver damage, sensitizes the liver to the toxic action of carbon tetrachloride, so that less of the latter is needed to cause death. It is apparently well established that most of the individuals who have died after small doses of carbon tetrachloride were chronic alcoholic addicts, presumably with preexisting liver disease. Chronic alcoholism in man seems to be a clearcut contraindication to the use of carbon tetrachloride.

Meat eating is another factor which has been shown experimentally to cause an acute exacerbation of the symptoms of carbon tetrachloride poisoning and a sharp rise in blood guanidine. Low glycogen reserve, or starvation, appears to decrease the tolerance to the drug. Oils and fats taken simultaneously with the drug cause a more rapid absorption of carbon tetrachloride.

At this point I should like to speak about the effect of oils on the toxicity of the anthelmintic drugs in general. Carbon tetrachloride, tetrachlorethylene and the other halogenated hydrocarbons are the only group of anthelmintic drugs, so far as I know, the toxicity of which is known to be increased by the simultaneous administration of organic oils or fats. It is generally stated that the toxicity of thymol is increased by oils, but this statement is based on a misquotation of the original work by Schultze published in 1915. Schultze concludes that "oils in which thymol readily dissolves greatly increased the dose necessary to kill," that is, reduced its toxicity. That is the statement which is generally misquoted. Hall has also shown in an experimental study that oils reduce the toxicity of aspidium, and the same is known to be true for hexylresorcinol and for oil of chenopodium. This matter is of considerable importance in the selection of a cathartic to be administered very soon after the anthelmintic agent, the choice lying usually between a

saline cathartic and castor oil. It would seem wise in the case of the carbon tetrachloride group that only a saline cathartic, such as magnesium sulfate, be used.

Tetrachlorethylene should logically follow carbon tetrachloride in the sequence of discussion. These substances differ considerably with respect to their toxic effects. Of the two, tetrachlorethylene has been shown to be very much less toxic to animals. It is less toxic to the liver even when given together with alcohol, seldom producing any degree of liver necrosis. Furthermore, calcium deficiency has been shown not to increase the toxicity of tetrachlorethylene, and there seems to be no doubt that it is a safer drug clinically. However, it may be considerably less effective as a vermifuge. It is very difficult to secure good evidence on that point.

As for oil of chenopodium, the margin of safety is not very large. Minor toxic symptoms are frequent and some deaths have been reported. The majority of deaths have followed overdosage in the usual sense, doses larger than those recommended for therapy. Here are some interesting comparisons: In normal cats the oral minimum lethal dose is 0.4 cc. per kilogram (equivalent to 24 cc. total for a 60 Kg. man). In starved, malnourished cats the oral minimum lethal dose is 0.15 cc. per kilogram (equivalent to 9 cc. total for a 60 Kg. man). The maximum therapeutic dose is stated to be about 3 cc., and in debilitated and anemic patients, using these figures as a rough measure of comparison, the margin of safety, as you can see, would not be great. Now if olive oil is administered with oil of chenopodium to starved cats the oral minimum lethal dose becomes 0.3 cc. per kilogram; that is, the toxicity is reduced. It is possible that serious poisoning by chenopodium is not seen frequently in man because it is customary to follow it with castor oil.

DR. HARRY B. RICHARDSON: Does it have to be an unsaturated oil?

DR. TRAVELL: Mineral oil, which is a mixture of saturated hydrocarbons, does not influence the toxicity of any of these anthelmintics. The experimental work has been done in the main with unsaturated oils, chiefly olive oil. Castor oil and cottonseed oil have also been shown to reduce the toxicity of some phenol derivatives.

The toxic effects of hexylresorcinol are of minor importance in the use of this drug. I am sorry that we do not have time to consider them now and hope that this topic will be discussed later.

DR. GOLD: We are fortunate in having Dr. Mackie with us this morning to lead the clinical discussion.

DR. THOMAS T. MACKIE: Before discussing the details of therapy for these different parasites I think it may be of some value to refer to their clinical importance. Beginning with the cestodes Taenia saginata and Diphyllobothrium latum, for the most part the indications for therapy are esthetic rather than purely clinical and medical. Taenia saginata does not produce disease. It may produce chronic indigestion, but it does not live strictly speaking at the expense of the host, and certainly not at the expense of the host's tissues. The reverse, however, may be true with respect to Taenia solium or pork tapeworm because under certain conditions the human being may become the intermediate as well as the definitive host. If a ripe proglottis is carried back into the human stomach by reverse peristalsis, the contained ova are liberated. The viable embryo then immediately penetrates the mucous membrane and is carried by the blood stream to different parts of the body, where it forms the pathologic response which is known as the cysticercus cellulosae. Fortunately, the pork tapeworm is exceedingly rare. Almost invariably the members of this genus that we see are Taenia saginata, but it is of some importance to know definitely in a specific instance which one we are dealing with, and there is a simple and easy method of identification with which many of you are probably familiar. That is simply taking one of the segments of the worm, placing it on a glass slide, placing another slide over it, pressing the two together, and holding it up to the light. The genitial orifice is visible on the lateral margin, the vaginal portion of the genital tract extending into the body of the worm joined by the two stem branches of the uterus. If the main collateral branches of the uterus are in the order of thirty or more per segment, we know that we are dealing with the nonpathogenic Taenia saginata; if they are fifteen or twenty, we know that we are dealing with Taenia solium, the pork tapeworm, for which we have an emphatic indication for therapy.

Diphyllobothrium latum was believed many years ago to produce a characteristic anemia, and in fact in one stage of the early work on pernicious anemia it was suspected that it might be one of the factors in producing this type of blood dyscrasia. That impression, however, has been thoroughly exploded. By way of illustration it may be of some interest to cite the fact that certain investigators have deliberately infected themselves with Diphyllobothrium latum, which they carried in their intestinal tracts for many months. Repeated observations of their blood counts throughout this period revealed no evidence of anemia.

As to the question of therapy, the anthelmintic drug most commonly used in the past in the treatment of cestodes is of course the extract of male fern or filix mas, that is, the oleoresin of aspidium. Unfortunately this is not particularly effective, and one has very many failures. It is recommended that the individual be placed on a starvation diet for a period of approximately two days before treatment. I question the necessity for that. It is likewise recommended that the individual be given a strong saline purge on at least two occasions within that period of forty-eight hours. I think there is a good deal of question about the necessity for that procedure. Oleoresin of aspidium is recommended to be given on an empty stomach on the third day in doses of 2 cc. in capsules at half hourly intervals for three doses. Some men who have worked in this field recommend that following the final dose approximately 2 cc. of spirit of turpentine be given likewise by capsule. This in turn is followed by a saline purge and two hours later by a large soap suds enema to ensure complete evacuation of the colonic contents.

It is further recommended that if the head is not obtained by such treatment the procedure be repeated again in approximately two to three weeks' time.

Probably a very much more effective method of approach is the use of carbon tetrachloride. As was emphasized a few moments ago, whenever this drug is used definite precautions have to be taken. We have to be sure that the individual has an ample amount of calcium in his blood stream. It is apparent that most individuals living on customary diets are none too well supplied with this mineral. It is important that the patient be on a high carbohydrate, low fat and low meat diet for a period of at least two or three days prior to treatment. It is important that alcohol be completely withheld during the period prior to treatment. It is important that food be completely withheld for a matter

of four or five hours after the drug has been administered and until catharsis has occurred in response to magnesium sulfate.

The roundworms fall into a different group from the point of view of therapy just as they do with respect to their biologic characteristics. Hookworm and its effects on the human organism are so well known that it is not necessary to emphasize the clinical picture, with perhaps this single reservation: There is a good deal of question in my mind as to the desirability of subjecting people to the potential hazard which treatment of these parasites entails unless we have evidence that the hookworms are actually producing some definite harm to the individual. That harm is evidenced first by the appearance of anemia. That is the most common response; and if, as is frequently the case in this part of the world, we see individuals coming back from the South who on stool examination show a few ova of Uncinaria but who are free from symptoms of any type and who have a normal hemoglobin and red cell count, it does not seem to me desirable to subject them to therapy because after a greater or longer period of time outside the endemic area they automatically become freed of the parasites which they carry.

Infection by the roundworm Ascaris is a different story, because these are large worms which are capable of producing serious damage in the host, but unlike the hookworm they do it mechanically. They are not strict parasites in the sense that they do not live on the host's tissues, but an adult ascaris may migrate into the appendix, it may and occasionally does migrate into the common bile duct, it may and occasionally does migrate up through the stomach, up the esophagus, and into the paranasal sinuses. I have seen a patient remove a large ascaris from his nose. Furthermore, in young children heavily infected, Ascaris may form a mass in the small intestine which can give rise to intestinal obstruction.

Occasionally a patient may carry a few of these worms, yet stool examination yields no evidence whatever to confirm their presence. That is, of course, due to the fact that male worms may be present and the gravid or egg-laying females absent.

The pinworm again lives one might almost say in symbiosis with its host. It does not destroy the tissues of the host. It may cause definite appendicular colic, especially in young children when single worms or groups of them reach the depths of the appendix. As has been pointed out previously, the treatment of this infection is exceedingly difficult for several reasons. In the first place the life cycle is not fully known. One finds statements in the literature that the period from ingestion of the ovum to the development of the fully gravid female requires from two weeks to two months. There is also evidence by analogy that what is technically spoken of as hyperinfection occurs; in other words, that under certain conditions the gravid female may lay her ova within the intestinal tract of the infected individual, and these ova there develop into the succeeding generation. The effects which are produced by this parasite are primarily the result of the cutaneous irritation produced by the migrating females as they emerge from the anus. These effects are disturbance of sleep, local skin irritation and the associated nervous phenomena which may occur especially in children.

The whipworm can cause definite lesions in the human colon. It customarily burrows into the mucosa, and cases of actual dysentery resulting from whipworm infestation have been described. They are, however, exceedingly rare. In most instances the symptoms associated with this infestation are so slight, and the hopes of effective therapy likewise so slight, that I do not feel that one is justified in attempting strenuous measures of therapy.

Again, we have a group of drugs which are applicable to the roundworms, that is to the nematodes, and which are not applicable to the cestodes. Carbon tetrachloride, already discussed, is an exception in that it is effective against both. In the past, oil of chenopodium was the drug of choice for the treatment of ascaris and hookworm infestations. It is given alone or in so-called mixed or combined treatments. The mixed treatment that is recommended is from 1 to 1.5 cc. of carbon tetrachloride for an adult, followed an hour later by 0.5 cc. of oil of chenopodium, and followed an hour later by an ounce of magnesium sulfate. The combined treatment consists of a single dose of small amounts of each of these two drugs, again followed shortly by a magnesium sulfate purge. Hexylresorcinol, however, is to be preferred to either.

The treatment of Oxyuris, the pinworm, is most unsatisfactory, and as has already been pointed out one of the most important factors is cleanliness. In the case of young children it may not only require careful cutting of the finger nails and scrupulous cleansing of the hands but it may mean even the wearing of gloves at night and the tying of the arms to the head of the bed so that the child cannot scratch. It requires the use of a mercurial ointment to the anal region at night, precautions concerning clothing and linen which may be contaminated, and repeated use of an effective anthelmintic drug. Recently, hexylresorcinol in doses of 1 Gm. for adults or from 0.6 to 0.8 Gm. for children has been reported to give very good results. This is given on an empty stomach and no food is permitted for five hours. Subsequently an enema of 0.1 per cent of an alkaline solution of hexylresorcinol is given and held for fifteen or twenty minutes. In practice, the oxyuris is by far the most difficult of all these infections to eradicate.

DISCUSSION

DR. GOLD: The conference is now open for general discussion. Dr. Smillie, would you care to make any comments?

DR. WILSON G. SMILLIE: The ideal anthelmintic is one that will remove all the parasites harbored without danger to the host at all. We have been looking for the ideal vermifuge for a long time, but it has never been discovered. I think we owe a great deal to Lamson, however, for his extensive pharmacologic studies on these vermifuges.

My recommendation is the use of hexylresorcinol. It will remove 90 per cent of Ascaris in a single administration without any danger to the host. It will remove from 75 to 85 per cent of the hookworms in a single administration. The great difficulty with oil of chenopodium is that its toxic dose is so close to its therapeutic dose. We treated over a million people in Brazil, in one country alone, with oil of chenopodium and had a very wide experience with its toxicity. We had some twenty-two deaths. Four persons to whom I had administered the drug died. Once you have seen a person die of oil of chenopodium poisoning you hesitate ever to give it again. It is a terrible death. The drug is one that has a special affinity for the central nervous system. Once the convulsions begin, lasting from twenty-four to thirty-six or forty-eight hours, while you must sit by and see the child finally die, is an awful experience. Carbon tetrachloride may also be quite

toxic. It is a very effective drug it is true, but it is dangerous. Some one mentioned the very first case of intoxication, which was described on a plantation in Brazil. That man recovered. I have had two deaths, however, from the drug, and here again it is a devastating experience, as you can well imagine, so that I do not recommend either oil of chenopodium or carbon tetrachloride. Tetrachlorethylene is as effective as carbon tetrachloride. Lambert in the South Sea Islands has now treated some 20,000 to 40,000 persons, and he has had no deaths as yet. His studies indicate that the drug is exceedingly effective. Hexylresorcinol has one great disadvantage, and that is it is expensive. Therefore it is quite impossible to use this drug on a wide scale among the poor people that are infected. It is a very serious matter of course, but nothing can be done about it. I should say then that hexylresorcinol, given in a single gram dose early in the morning on an empty stomach, followed within an hour to an hour and a half by a saline purge, with no food taken until noon, is by far the most satisfactory method of anthelmintic therapy we have at the present time. Tetrachlorethylene is given in 3 cc. doses on an empty stomach, in the early morning following a light supper. No breakfast is eaten. The drug is given at 7 o'clock in the morning; 1.5 cc. is taken in hard gelatin capsules, followed an hour later by another 1.5 cc. and followed an hour later by a purge of magnesium sulfate. The results are splendid.

Some one mentioned the reduction in toxicity of oil of chenopodium when given with oils. The quickest way to kill a dog is to give him a mixture of a little oil of chenopodium with bile. If you mix the drug with castor oil, however, it is relatively safe, and so if you must give oil of chenopodium I would recommend that you administer, to a child with Ascaris, 0.5 cc. with a tablespoonful of castor oil. Mix the two together, and you will get excellent results with little danger of intoxication.

The worm that can be most easily removed is Ascaris. The next is the hookworm. The pinworms, as has been said, are difficult to remove. The whipworms, because they thread themselves through the mucous membrane, are very hard to remove. Actually, as Dr. Mackie says, it is not necessary often to get them.

DR. GOLD: Is there any other discussion?

DR. MCKEEN CATTELL: Have there been no untoward effects found to follow the use of hexylresorcinol?

DR. SMILLIE: Yes, in children that chew up the capsules. They get a burning sensation of the mouth. It is very disagreeable, so the drug is put up in an iron-bound capsule which the child will find impossible to chew. Once it gets into the stomach there may be a slight burning sensation, but no serious toxic results follow.

DR. TRAVELL: Dr. Lamson has published a study on dogs in which he examined the gastrointestinal tracts after giving hexylresorcinol to see what happens in the stomach when the capsule is not chewed up. He reported submucous hemorrhages and also superficial ulceration of the gastric mucosa; but he found that the ulcerations were transient and had practically healed within seventy-two hours, leaving no permanent lesions. He also carried out a study on a large series of alkylphenols to try to find one that would be less irritant than hexylresorcinol and he came to the conclusion, using the pig ascaris as a test object, that the ascaricidal action could not be divorced from the irritant action and that any procedure, such as the giving of oil, which tended to reduce the irritant action of hexylresorcinol also greatly reduced its effect on the parasites.

DR. MACKIE: I have used the drug in Guatemala in much larger than the recommended dosage without any evidence of toxic symptoms other than the complaint of some epigastric burning for an hour or an hour and a half after administration.

DR. GOLD: This is hexylresorcinol?

DR. MACKIE: Yes.

STUDENT: Is hexylresorcinol good for flatworms?

DR. SMILLIE: No, not very effective for flatworms.

VISITOR: Would a question in differential diagnosis be out of order here? I should like to know what Dr. Mackie thinks regarding the skin test material which I believe is put out by Lederle to differentiate between these two types of worms, particularly when repeated stool examinations have failed to identify the parasite.

DR. MACKIE: It is not a very dependable or a very worth while method of diagnosis. I do not think it is particularly practical.

DR. SMILLIE: If you cannot find the ova in the stools it does not make any difference anyway, for the infection is so light that it is not of practical importance. There is one point that ought to be emphasized in therapy, and that is clearly brought out in the studies of Rhoads and Castle in Puerto Rico. After you remove hookworms in a heavily infested person the child will not get well unless you give him large amounts of iron. Give it to him in large doses in the forms in which it is readily available. In their Puerto Rico experiments they were willing to recommend, if they had to make a choice between iron and the anthelmintic, to give the iron and forego the anthelmintic. The child builds up hemoglobin rapidly even though the worms are continually taking the blood. The sensible thing to do is to get rid of these worms and then give the patients large doses of iron; but the customary method of giving the anthelmintic and then expecting the child to get well is not good therapy, because they must have large amounts of readily available iron to secure prompt recovery.

DR. GOLD: Is there a toxin liberated by the hookworm?

DR. SMILLIE: No, it was thought for many years that the hookworm produced a toxin, but all of Castle-Rhoads' studies show the anemia is due purely to loss of blood. Wells, working with the dog, in studies in which he opened the intestine of the dog and watched the living worm in gross, found that this worm not only sucked blood for digestion but that there was also a continued stream of blood flowing through the worm.

DR. JOHN E. DEITRICK: Is there anything new in the management of trichinosis? We still see that in New York, probably more commonly than any of these other worms.

DR. TRAVELL: Better control of the kind of garbage that is fed to pigs.

DR. MACKIE: Better control of cocktail canapés.

DR. DEITRICK: There seems to be little we can do for these patients.

DR. SMILLIE: Some recommend giving an anthelmintic, but the results are rather doubtful because by the time you see the patient the damage is done and you cannot reach the worms. Any vermifuge that has ever been discovered that can be used to kill the worm in the general circulation is toxic to the host. Lambert tried that. He used three cannibals that were convicted

to be shot. He gave one oil of chenopodium intravenously with disastrous results. He gave intravenous vermifuges to the others as well, but even small doses in the circulation are toxic.

DR. DEITRICK: Is it true that the adult trichinae will persist in the intestinal tract for two or three or four weeks?

DR. SMILLIE: Yes, but they are not within the intestinal tract. They are buried deeply in the mucosa.

DR. DEITRICK: When a patient with trichinosis is admitted, we give him a large dose of magnesium sulfate and attempt to clean out as many of the worms as possible. That is practically all we can do.

DR. SMILLIE: It is perfectly reasonable therapy. I would also suggest that tetrachlorethylene be given because you cannot do the patient any harm and you may get some of the adult worms.

DR. GOLD: Am I correct in assuming that both Dr. Smillie and Dr. Mackie prefer hexylresorcinol to oil of chenopodium for the treatment of roundworms?

DR. MACKIE: Yes. I think it is much the safest.

DR. SMILLIE: For effectiveness, oil of chenopodium is in a class by itself. A dose of 1.5 cc. is perfect. One can remove from 90 to 95 per cent of the worms in a single dose, but it is dangerous. That is the trouble.

DR. GOLD: If there are no further questions, we will adjourn.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

CEVITAMIC ACID-LEDERLE (Ascorbic Acid-Lederle) (See New and Nonofficial Remedies, 1939, p. 500).

The following dosage form has been accepted:

Tablets Ascorbic Acid-Lederle, 0.025 Gm.

SALYRGAN-THEOPHYLLINE SOLUTION.—Mersalyl-Theophylline Solution.—A solution containing 10 per cent by weight of sodium [o(hydroxy-mercuric-methoxy-propylcarbamyl) phenoxy] acetate and 5 per cent by weight of theophylline.

Actions and Uses.—Salyrgan-Theophylline Solution has been demonstrated to produce less local reaction on intramuscular injection than salyrgan alone and to be somewhat more effective. It is believed that the more rapid resorption of salyrgan in combination with theophylline accelerates diuresis and, by preventing the deposition of mercury, improves the local tolerance. Salyrgan-theophylline solution is proposed as a diuretic for dropsy in cardiorenal disease and in nephrosis, ascites of liver diseases and other conditions. It is contraindicated in acute nephritis and chronic kidney disease in an advanced stage with marked tubular and glomerular changes; also intestinal inflammation with diarrhea. As do other mercurials, salyrgan-theophylline solution may give rise to side effects, particularly stomatitis, gastric disturbance, more or less diarrhea, vertigo, headache, febrile reaction and cutaneous eruptions. When the use of salyrgan-theophylline is continued over a prolonged period of time the urine should be examined from time to time for albumin, casts and blood cells.

Dosage.—For Adults: For susceptibility test of patient the first dose should be 0.5 cc. If well tolerated, the dose may be increased to 1 cc. on the following day. In some cases 2 cc. may later be required for the full effect. Usually injections are not given more frequently than every three or four days. After relief of the dropsy, recurrences can often be prevented by occasional injections. For Children: The dose for children of salyrgan-theophylline is proportionately less than that for adults (0.25 cc. to test susceptibility, followed by 0.5 or 1 cc. the following day).

Manufactured by Winthrop Chemical Company, Inc., New York. "Salyrgan" U. S. patent 1,693,432 (Nov. 27, 1928; expires 1945). U. S. trademark 188,515.

Ampoule Solution Salyrgan-Theophylline, 1 cc.: Each cubic centimeter contains salyrgan 0.1 Gm. and theophylline 0.05 Gm.

Ampoule Solution Salyrgan-Theophylline, 2 cc.: Each cubic centimeter contains salyrgan 0.1 Gm. and theophylline 0.05 Gm.

Salyrgan-theophylline solution is an aqueous, colorless, odorless, bitter solution, of slightly alkaline reaction. The *p*H of the solution is approximately 7.8 (±0.2). To differentiate from salyrgan solution, add 0.5 cc. of acetic acid to 5 cc. of salyrgan-theophylline solution: no immediate precipitation takes place. Add 3 cc. of formic acid to 5 cc. of salyrgan-theophylline solution: a white precipitate is formed which, on boiling, dissolves, leaving a gray residue of metallic mercury. Add 10 cc. of distilled water and 10 cc. of diluted hydrochloric acid to 3 cc. of salyrgan-theophylline solution; boil for ten minutes and cool; extract the resulting salicyl allyl amido acetic acid with 20 cc. portions of ether; evaporate off the ether and dry the residue over phosphorus pentoxide in a vacuum desiccator: the melting point of the residue (salicyl allyl amido acetic acid) is from 120 to 121 C. Through the aqueous phase from which the salicyl allyl amido acetic acid has been extracted, bubble sufficient hydrogen sulfide gas to precipitate all mercury; filter and evaporate the filtrate to 20 cc.; after cooling, add 10 Gm. of sodium acetate; extract the solution in a small liquid-liquid extractor with 30 cc. of chloroform; evaporate off the chloroform and dry the residue (theophylline) in a desiccator of sulfuric acid: the melting point of the residue is from 269 to 272 C. The residue gives the murexide reaction (U. S. P. XI, page 384). Add 1 cc. of silver nitrate test solution to 1 cc. of salyrgan-theophylline solution: a white precipitate of silver-theophylline results which does not go into solution on addition of 2 cc. of diluted ammonium hydroxide solution. Add 0.5 cc. of diluted acetic acid (1: 1) and 0.3 cc. of sodium sulfide water to 5 cc. of salyrgan-theophylline solution: only a very faint coloration of the solution is noticeable.

ASSAY FOR SALYRGAN: To 5 cc. of salyrgan-theophylline solution in a 250 cc. beaker add slowly 10 cc. of sulfuric acid. Warm on a steam bath and add cautiously at five minute intervals four 0.5 cc. portions and one 2 cc. portion of a 30 per cent hydrogen peroxide solution. Heat for at least one hour after the last addition of hydrogen peroxide: the solution is colorless. Add 50 cc. of water and potassium permanganate solution in slight excess. Decolorize with oxalic acid solution. Add 10 cc. of concentrated sulfuric acid, 2 cc. of ferric ammonium sulfate T. S., and make up the total volume to 100 cc. with water.

Prepare a control. To 78 cc. of water add 20 cc. of sulfuric acid, 2 cc. of ferric ammonium sulfate and 0.05 cc. of N/10 potassium thiocyanate solution. Titrate the diluted salyrgan-theophylline solution with N/10 potassium thiocyanate solution to the same intensity of color: each cubic centimeter of N/10 potassium thiocyanate solution used is equivalent to 0.02528 Gm. of salyrgan; the amount of salyrgan corresponds to not less than 9.5 per cent nor more than 10.5 per cent.

ASSAY FOR THEOPHYLLINE: To 5 cc. of salyrgan-theophylline solution in a 200 cc. Erlenmeyer flask add 1 cc. of sulfuric acid and 50 cc. of water. Bubble hydrogen sulfide gas through the solution until the mercury is precipitated in the form of mercury sulfide. Remove the excess hydrogen sulfide by boiling and filter while still warm. To the filtrate and washings in a 200 cc. Erlenmeyer flask add 5 Gm. of ammonium acetate and 20 cc. of N/10 silver nitrate solution. Evaporate until the volume has been reduced to 50 cc. Filter with vacuum while still warm. Wash the resulting cake with three 10 cc. portions of water. Add 5 cc. of nitric acid to the washings and filtrate. Add 2 cc. of ferric ammonium sulfate T. S. and cool. After cooling, titrate the excess silver with N/10 potassium thiocyanate: each cubic centimeter of N/10 silver nitrate indicates the presence of 0.0198 Gm. of theophylline; the amount of theophylline corresponds to not less than 4.75 per cent nor more than 5.25 per cent.

ESTRONE (THEELIN) (See New and Nonofficial Remedies, 1939, p. 345).

Estrone-Lilly.—A brand of estrone (theelin)-N. N. R.

Manufactured by Eli Lilly & Co., Indianapolis, by license from St. Louis University under U. S. patents 1,967,350 and 1,967,351 (July 24, 1934; expire 1951). No U. S. trademark.

Ampoules Estrone, 0.1 mg. in oil, 1 cc.: Each cubic centimeter contains estrone 0.1 mg. (1,000 international units) in a bland vegetable oil.

Ampoules Estrone, 0.2 mg. in oil, 1 cc.: Each cubic centimeter contains estrone 0.2 mg. (2,000 international units) in a bland vegetable oil.

Ampoules Estrone, 0.5 mg. in oil, 1 cc.: Each cubic centimeter contains estrone 0.5 mg. (5,000 international units) in a bland vegetable oil.

Ampoules Estrone, 1.0 mg. in oil, 1 cc.: Each cubic centimeter contains estrone 1.0 mg. (10,000 international units) in a bland vegetable oil.

Vaginal Suppositories Estrone, 0.2 mg.: Each suppository contains estrone 0.2 mg. (2,000 international units) in a glycerin base.

ESTRIOL (THEELOL) (See New and Nonofficial Remedies, 1939, p. 347).

Estriol-Lilly.—A brand of estriol (theelol)-N. N. R.

Manufactured by Eli Lilly & Co., Indianapolis, by license from St. Louis University under U. S. patents 1,967,350 and 1,967,351 (July 24, 1934; expire 1951). No U. S. trademark.

Pulvules Estriol, 0.06 mg.: Each pulvule contains estriol 0.06 mg.

Pulvules Estriol, 0.12 mg.: Each pulvule contains estriol 0.12 mg.

Pulvules Estriol, 0.24 mg.: Each pulvule contains estriol 0.24 mg.

RIBOFLAVIN (See New and Nonofficial Remedies, 1938, p. 479).

Riboflavin-Merck.—A brand of riboflavin-N. N. R.

Manufactured by Merck & Co., Inc., Rahway, N. J. No U. S. patent or trademark.

Ampule Riboflavin-Merck, 10 mg.
Ampule Riboflavin-Merck, 100 mg.
Riboflavin-Merck, 1 Gm. Bottle

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SATURDAY, JULY 29, 1939

TUBERCULOUS TRACHEOBRONCHITIS

Eppinger [1] in 1881 gave the first complete anatomic description of tuberculous tracheal ulceration, pointing out the tendency of the ulcers to localize in the lower part of the trachea. In about one eighth of his necropsies the lesions were not associated with tuberculous laryngitis. He believed they were an extension from the adjacent tuberculous lung tissue and caseating peribronchial lymph nodes. Despite this excellent description, tracheobronchitis as a complication of pulmonary tuberculosis received but scant attention in the succeeding decades. With the revival of interest in tracheobronchial tuberculous disease, a number of studies of necropsy material have become available. Reichle and Frost,[2] on the basis of microscopic examination of the tracheobronchial tree in thirty-seven cases in which death occurred from chronic phthisis, concluded that the common modes of infection of the major bronchi are by contiguity from the diseased lymphatics and lymph nodes of the peribronchial tissue or by continuity occurring secondarily to an implantation tuberculosis in the lower lobe and in the bronchi draining a tuberculous cavity. They considered implantation the least important mechanism of invasion of the tracheobronchial mucosa, particularly in the case of the larger bronchi because of the protective influence of the cilia, mucus and bronchial peristalsis. Bugher, Littig and Culp [3] studied 122 cases of pulmonary tuberculosis at necropsy. In their experience, extension from peribronchial tissue was not an important mechanism. They state that in no instance of tracheotuberculosis did they find diffuse peritracheal tuberculosis and that lesions of the tracheal mucosa occurred without tubercles being found in the adjacent peritracheal lymph nodes. They conclude that extension from the peritracheal tissue did not assume an important role. They were impressed with the tendency of the lesions to occur with great frequency on the posterior wall in patients who had been recumbent for long periods. The fact that the sputum was rich in tubercle bacilli in all these cases further emphasized the probable role of implantation. While laryngeal tuberculosis was frequently concurrent with tracheobronchial tuberculosis (76 per cent of their cases), it was considered by them as not causally related.

Recent advances in roentgenology and bronchoscopy together with a renewed interest on the part of the phthisiatrists have led to clinical recognition of tuberculous tracheobronchitis. Its presence is to be suspected when a patient exhibits a persistent wheeze and rattling, asthmatoid attacks, erratic rises in temperature not associated with extension of the pulmonary disease, paroxysms of violent coughing, dyspnea and cyanosis on slight exertion, excessive amount of a tenacious sputum rich in tubercle bacilli, and a great variation in its amount from day to day. Roentgenograms are likely to reveal lobar or total pulmonary atelectasis with or without collapse therapy. Total pulmonary atelectasis taking place rather abruptly after induction of a pneumothorax is suggestive. Roentgenograms may further demonstrate an unexpected spread of a tuberculous infiltration or a rapid enlargement of a cavity.

The recent contributions of Clerf, Tucker, Myerson, Samson and others have demonstrated the relative innocuousness of bronchoscopy in pulmonary tuberculosis, as well as its value in the recognition and to some extent in the treatment of tuberculous tracheobronchitis and its complications. Diagnostic bronchoscopy is, however, contraindicated in the presence of hemoptysis, severe laryngeal ulceration or hopeless pulmonary disease. McIndoe and his co-workers [4] concluded, after an experience of two years during which 272 patients were examined, that routine bronchoscopic examination is not necessary for the discovery of significant tuberculous tracheal and bronchial lesions. Bronchoscopy in their opinion should be performed only when suggestive signs or symptoms are present. Bronchoscopy did not have a deleterious effect on any patient in their group.

Tuberculous tracheobronchitis definitely aggravates the pulmonary disease. Climatic treatment, ultraviolet rays, tuberculin therapy and roentgen therapy have not thus far contributed much to the amelioration of this condition. Major collapse therapy is rather to be avoided in cases complicated by tracheobronchial ulceration, since it may further add to the already existing difficulty in raising the sputum and to the respiratory embarrassment. According to Samson,[5] symptomatic improvement has followed in select cases the bronchoscopic aspiration of retained secretions, chemical shrinkage of edematous mucosa or the cautious dilation of circumscribed bronchial stenoses.

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VITAMIN K

Clinically active vitamin K has been obtained principally from putrefied fish meal and alfalfa meal. In 1933 Anderson and Newman [1] isolated a pigment from human tubercle bacilli which they designated phthiocol and the chemical constitution of which was determined as 2-methyl-3-hydroxy-1,4-naphthoquinone. The synthetic preparation of this quinone was tested by Almquist and Klose,[2] who found that it possessed antihemorrhagic activity similar to that of vitamin K. The term phthiocol however has not been adopted generally by all other American or foreign investigators of this field or by the Council on Pharmacy and Chemistry. The preparation and purification of crystalline concentrates have proceeded rapidly and purified products have been announced almost simultaneously in many different laboratories. From Europe in March of this year a report appeared by Dam, Karrer and their colleagues [3] on the isolation of vitamin K from alfalfa. There seems to be now general agreement that the vitamin contains a quinone structure. Thus Almquist and Klose declare that the antihemorrhagic activity of phthiocol lies between that of the methyl naphthoquinone and the hydroxy naphthoquinone. Ansbacher and Fernholz [4] found, in confirmation, that 2-methyl-1,4-naphthoquinone is practically as active as vitamin K.

Fieser and his colleagues,[5] from experiments with various quinones on day-old chicks, suggest that some of the 2-hydroxy-3-alkyl-1,4-naphthoquinones possess positive vitamin K activity. In spectographic data reported also by Fieser and his co-workers [6] there is close correspondence indicated between the natural vitamins and model substances of the postulated structure of 2,3-dialkyl-1,4-naphthoquinones.

Similarly the most recent work of MacCorquodale, Binkley, Thayer and Doisy [7] led them to the belief that the structure of the vitamin K_1 molecule is 2-ethyl-3-phytyl-1,4-naphthoquinone. Obviously this work of chemical identification has advanced to the point at which one can be reasonably certain that at least much of the activity of what is now considered due to vitamin K can be attributed to one or more quinone derivatives. It seems by no means certain as yet, however, that the various substances crystallized and identified are identical in action, although it can be confidently anticipated that this question will soon be resolved.

Much of the recently acquired clinical information on vitamin K is adequately summarized elsewhere in this issue in the articles by Smith and his associates [8] and by Butt and his associates.[9] Conclusions cannot now be drawn as to the relative clinical activity of the more purified products so recently discovered. Furthermore, the naming of the final purified active crystalline product which will represent the efforts of such a large group of investigators must be carefully considered in order to conform to the best principles of scientific terminology and the avoidance of any therapeutically suggestive designation.

CELLULAR RESPIRATION

Lavoisier's conception of respiration was the combustion of foodstuffs through oxygen. Although foodstuffs are oxidized by the body cells at relatively low temperatures, they do not react readily with oxygen in the laboratory. Powerful oxidizing agents are required to duplicate the combustion which occurs so readily in the organism. In view of this difference, the mechanism of cellular oxidation has long puzzled investigators. Work on this problem has been discussed in recent reports by Barron [1] and by Szent-Györgyi.[2] There are several ways in which the oxidation of a substance may be effected; addition of oxygen or removal of hydrogen accompanied by withdrawal of electrons, or simply removal of electrons without addition of oxygen or removal of hydrogen, results in oxidation. The cell is capable of oxidizing metabolites with the help of catalytic systems, oxidation being accomplished by means of a series of oxidation-reduction reactions involving a variety of substances in the tissues.

Since oxygen does not readily attack molecules of absorbed food materials at the comparatively low temperature of the body, the process must be activated in some way in order to proceed at this temperature. One of the first links in a chain of such reactions was described by Warburg, who discovered an enzyme capable of activating molecular oxygen. Another important contribution was made by Keilin, who showed that certain pigments present in cells and called "cytochromes" are involved in cellular respiration. Three cytochromes have been described, and there is an iron atom in at least one, and probably in all of them. This metal atom is the active constituent of the molecule; in respiration it is susceptible of being alternately oxidized and reduced. A cytochrome, prepared in pure form, was not oxidized by atmospheric oxygen at a measurable rate. Important from the aspect of cellular respiration, however, is the fact that oxidation may be effected by an oxidase which is either identical with

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9. Butt, H. R.; Snell, A. M., and Osterberg, A. E.: The Preoperative and Postoperative Administration of Vitamin K to Persons Having Jaundice, this issue, p. 383.

1. Barron, E. S. Guzman: Cellular Oxidation Systems, Physiol. Rev. **19:** 184 (April) 1939.
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Warburg's respiratory enzyme or similar to it. In the cell also are enzymes called dehydrogenases. These act on metabolites in such a way that certain hydrogen atoms become labile and amenable to being readily removed by a suitable acceptor (oxidizing agent). Consequently a typical oxidation-reduction reaction may take place, the metabolite being oxidized and another substance being reduced. The reduced material may then in turn be oxidized by still another substance. Thus there is a chain of electron transfers in which hydrogen of the foodstuff serves as an electron donator, substances such as the cytochromes act as electron transmitters, and oxygen behaves as the ultimate electron acceptor. Cellular respiration is therefore simply the process by which the cell extracts energy from the molecules of food materials, the release of energy depending on the foregoing series of reactions. Szent-Györgyi has emphasized the role that may be assumed by such simple metabolites as fumaric and succinic acids as intermediary carriers in cellular respiration. Oxidation-reduction systems involving phosphoriboflavin-protein and diphosphorpyridine-nucleotide have also received attention and are of considerable importance in biologic oxidation processes.

Cellular oxidation is conceived as occurring in stages, the system of more negative potential being oxidized by the reduction of the system of more positive potential in a series of graded steps up to the reduction of molecular oxygen. Like locks in a canal, as Barron describes it, these reversible systems gradually release the oxidation energy. Oxygen as the ultimate hydrogen acceptor in cellular oxidation is reduced to form water, one of the end products of cellular respiration. In which step of the oxidation-reduction series the other end product, carbon dioxide, appears is scarcely known. Some of it may arise through intermolecular oxidation-reductions of ketonic acids, some by the interaction of α-ketonic acids and amino acids, some by the oxidation of pyruvic acid and other similar processes.

A recent addition to our knowledge in the field of cellular respiration is the observation that certain vitamins have an important part in processes of biologic oxidation. Riboflavin, for instance, is known to form an integral part of an oxidation-reduction system and presumably is a dietary essential because it is required by the body for the formation of this system. Likewise diphosphothiamin is known to be involved in a system effecting the oxidation of pyruvic acid, and nicotinic acid amide has been found to be a structural unit of a coferment which is thought to play a part in oxidation-reduction reactions in the cell. The therapeutic properties of nicotinic acid in cases of pellagra are due, according to Spies, at least in part, to its effect on codehydrogenase.[3]

Much of our knowledge of possible mechanisms of cellular respiration has been obtained as the result of a study of isolated enzyme systems. Strictly speaking, the results hold only for the conditions for which they have been worked out. These studies have, however, given an insight into the mechanisms involved in cellular oxidation and afford information concerning the role of some vitamins as essential components of enzymes involved in fundamental biologic reactions.

3. Stafford, Jane: Nicotinic Acid and Pellagra, Science **89:** 12 (April 7 supp.) 1939.

Current Comment

WHAT IS OSTEOPATHY?

In the State Board issue of THE JOURNAL the question What is Osteopathy? was asked.[1] One answer is found on page 447 of this issue. Osteopathy is a system of therapy without benefit of operative surgery or the use of drugs as remedial aids. In Kansas the osteopaths procured the enactment in 1913 of legislation that authorized adherents of the cult to practice osteopathy as taught and practiced in legally incorporated colleges of osteopathy of good repute. Proponents of the legislation evidently thought that they had thus found an easy way to obtain the unlimited right to practice medicine without qualifying themselves as legitimate practitioners of medicine must do. All that was necessary, they apparently thought, was for osteopathic schools to add a bit of materia medica and operative surgery to their courses and thenceforth osteopaths would be entitled to practice medicine and surgery. Quite a simple procedure! Only it did not work! The Kansas court in the case abstracted in this issue emphasized the fact that a law is to be construed as of the time of its enactment. The use of drugs as remedial aids and the use of operative surgery, the court pointed out, formed no part of the practice of osteopathy in 1913 when the act was passed. The fact that schools of osteopathy may have since introduced instruction in those branches of medicine does not enlarge the scope of osteopathic practice. Osteopaths in Kansas, therefore, have no right to employ such agencies. That the court correctly interpreted the legislative intent in passing the osteopathic act is evidenced by the fact that the recent Kansas legislature, subsequent to the decision of the court, denied the importunities of osteopaths for legislation granting them extensive privileges in the field of medicine, the legislature being unconvinced that osteopaths were qualified to practice operative surgery with instruments and to use drugs. In several other states, including Georgia, Missouri, Nebraska, New Mexico and North Carolina, osteopaths have obtained the enactment of legislation containing phraseology similar to that used in the Kansas law. The Kansas decision is commended to the careful consideration of those states. The decision is of importance too in those states in which osteopathic laws do not specifically define what constitutes osteopathy, such as Arizona, Delaware, Idaho and Mississippi. The Supreme Court of Kansas has rendered a distinguished service to the people of the state in thus thwarting the efforts of a group of substandard healers to edge into the field of the practice of medicine through the back door.

1. What Is Osteopathy? editorial, J. A. M. A. **112:** 1728 (April 29) 1939.

ORGANIZATION SECTION

CONFERENCE ON MEDICAL PATENTS

(Concluded from page 336)

MANUFACTURERS' POINT OF VIEW ON MEDICAL PATENTS IN RELATION TO PUBLIC WELFARE

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While listed on the program as presenting the manufacturers' point of view on medical patents in relation to public welfare, I wish to make it clear at the start that I am not undertaking to speak for the pharmaceutic industry. The majority of manufacturers might or might not agree with my views as expressed, which are purely personal but naturally based on such experience as I have had in the industry.

I presume that the motive underlying the calling of this conference has to do less with the advantages or disadvantages of our patent system than it does with the policy which should be encouraged, particularly in medical schools, with regard to their securing and owning patents and their administration when secured and owned.

However, one can hardly divorce these specific questions from the general philosophy of the patent system.

The general aspects of the patent situation and the relation of patents to social and economic progress have been discussed so often and so well as to require little additional comment.

Aside from the interesting discussions that have taken place today, I have no doubt that most of you either heard or subsequently read the presentations of Dr. Fishbein, Mr. Schley, Dean Russell and others in the symposium held under the auspices of the American Chemical Society at Rochester in September 1937. These various men reviewed most admirably the questions involved and there is little to be said to a group of this kind which is either new or novel. My discussion must necessarily be little more than an expression of agreement with some of the thoughts (not all of them) that have been repeatedly expressed by others.

Before taking up the relationship of patents to the public welfare, I should like to digress long enough to consider briefly the question of equity of the inventor. This is a subject perhaps less interesting to those associated with medical schools and other medical organizations than it is to industry. To one, however, who believes in the enterprise principle as applied to American life, it does not seem unreasonable to hold to the principle that the inventor (whether it be a firm that has spent years in research on a certain project and large sums of its stockholders' money or whether it be an individual who has given perhaps the best years of his life to the pursuit of some particular problem) should not go unrewarded when these efforts result in practical achievement. To deny this seems to me to deny the soundness of vital factors in the character and accomplishments of the American people. To refuse to any branch of industry—and this I contend applies to the pharmaceutic as well as any other—the opportunity to improve its business position by capitalizing the discoveries that it has made, or assisted to be made, would represent a departure from the principles which have had a large share in the progress of our business institutions and which have had important resultant effects on the progress of the nation.

There are some who may not agree as to the general advantages of the patent system but who in any event oppose the taking of patents on discoveries which fall within the field of medicine. Again, this is a subject which has been repeatedly and ably discussed. However, it is so fundamental that I wish to comment briefly on certain phases of it.

The chief objection which is offered to medical patents is not dissimilar to that advanced against the patent system generally, namely that patents lead to monopoly. It is argued that monopoly as a result of patent control is particularly undesirable in the case of medical preparations.

Monopoly as a result of patent ownership is an obvious possibility in medical just as well as with other patents. In considering this matter as related to medical products, however, it is well to examine the matter historically and see whether or not monopoly has been a matter of great practical significance. I think that an unbiased review of the facts will reveal that monopoly for the most part has been a theoretical rather than a practical consideration.

Only occasionally is a patent sufficiently broad in scope to cover any therapeutic field. Examples of such broad patents are the insulin patent and the scarlet fever patent, the administration of which has been reviewed by previous speakers. Neither of these patents, of course, was administered on a monopolistic basis. Usually patents on pharmaceutic or biologic products cover only a segment of the field and do not open up the possibility of eliminating competition. To illustrate, there are probably a dozen patents covering antianemic preparations but, nevertheless, it is a highly competitive market. There are many patents on mercurial antiseptics, bismuth compounds, arsenicals and vitamin preparations. Still these fields are all very actively competitive. For most patented products there are equivalents or sufficiently near equivalents to put the products in active competition. A manufacturer may enjoy a temporary advantage but it is usually not long before one or more of his competitors bobs up with a product which will serve the same purpose. Those of you who are engaged in the practice of medicine have but to review the patented products that you are using for this to be apparent. Those who represent pharmaceutic houses and have had experience in introducing new pharmaceutic products I am sure do not need to be convinced on this point.

I have previously referred to the protection of the equity of the inventor assured by our patent system. However, we all recognize that the chief objective of a patent system is not the rewarding of inventors or their sponsors. The object sought is the promotion of discoveries and inventions which will contribute to the public welfare. If this were not so, I have no doubt that patents would long since have become extinct for the reason that even in our democratic country society is much less interested in rewarding individual effort than it is in improving the common welfare.

In expressing the conviction that it has been a very important factor in the progress of the science of medicine, I do not advance the theory that the patent system is a sine qua non to research progress in medicine. We all know that many great discoveries have come from institutions and individuals with no patent interest whatever. The spirit of investigation is a part of the very warp and fabric of medicine.

Nevertheless, the patent system has been a driving force toward invention. Not particularly so with regard to medical men, but with others—especially chemists—whose activities are importantly related to the science of medicine.

We cannot ignore entirely human instincts or assume that the research worker, because he has an unselfish desire to contribute knowledge and service to humanity, must consider that he should therefore be improvident in his attitude toward his own future and the future of his family. I think it is fortunate not only for the chemist but also for society that he has not been shackled with inhibitions about patents because I am sure that otherwise many important discoveries would have been lost to mankind.

Aside from this fundamental matter of incentive, there is another important consideration which enters into this general picture, and that is the free disclosure of scientific work which

is encouraged by patents. There are probably few practical achievements in science which are purely individual. Most of the important accomplishments are made possible by knowledge developed by prior workers. It is true that the man who carries out the final step often reaps a reward out of proportion to the part he has played in the whole development. Nevertheless, the public welfare is served by the fact that a practical achievement has been reached. The far greater element of secrecy which would exist in the absence of a patent system would unquestionably be a great deterrent to scientific progress.

The patent system also fosters the development of research institutions affiliated with or supported by commercial laboratories. The activity of such research divisions is a consequential factor not only in regard to direct contributions but in cooperating with research laboratories in universities and elsewhere. Furthermore, such research departments are important in the transition of discoveries from their original state to that of practical utilization. There is the further fact that the existence of research laboratories affiliated with pharmaceutic and biologic manufacturing plants has had a very definite influence in raising the standards for manufacturing pharmacy and the promotion of constantly more rigid methods of standardization.

It would, of course, be ridiculous to assume that the research departments associated with such companies would languish and die in the absence of a patent system. Patents or no patents, such research would go on. There is, however, no gainsaying the fact that in the absence of some method of protecting the fruits of research we should not have had the same development in the past as has taken place; neither would there be the same motivation for continuing expansion.

The policy of pharmaceutic manufacturers is generally and definitely to protect their discoveries by patents. The majority of universities and colleges, on the other hand, to a large extent lack any definite policy. Some of them are vigorously opposed to patents on discoveries by members of their faculties of medicine. They regard taking patents as a step down from the ideals and traditions of medicine.

This state of mind is perhaps a natural result of that ingrained sense of service to humanity which distinguishes the profession of medicine. There is a deep-seated feeling that those high ethical standards which have glorified the doctor for countless generations must not be compromised.

One cannot do other than admire this stalwart adherence to ideals and hope that the principles which have maintained the medical profession on its high plane of service to humanity will always endure.

One can, however, disagree with the conclusion that aloofness on the part of medical institutions in the matter of patents is the only way, or even the best way, of accomplishing the greatest service to humanity in the matter of important discoveries. If we approach the subject realistically and not sentimentally, I think we shall find ample support for the conclusion that patents secured by medical schools may be so administered, and are being so administered, as not only to avoid conflict in the slightest degree with the ideals and traditions of medicine but, on the other hand, to be a strong constructive influence in their support.

It is of course obvious, to begin with, that patents controlled by universities and licensed to manufacturers often provide, through royalty, substantial sums of money for the promotion of new research. If this were the only consideration, however, it would not be difficult to understand why certain universities and colleges would not be interested in patents. Deriving additional revenue, even for research purposes, does not always loom up as a sufficiently important consideration for them to depart from time-tried policies.

This is not, however, the most important consideration: failure on the part of the university to take a patent may result in patent control passing into the hands of others who would not administer it with the same broad interest that would be exercised by the university. It by no means follows that the research worker, in publishing his work, gives his discovery to the world even though that is his intention. Omissions which he may easily make (not being patent minded) have the result that his publication is not a barrier to some one else securing a patent on some important phase which may dominate the situation. After the unselfish American scientist has done the fundamental work, mass attacks on vital processes, organized in some instances not only on a national but even an international scale, may transfer the control from the American discoverer to such interests.

Another important consideration in university patents is the matter of product control. In the case of universities who own patents which they administer by license to pharmaceutic manufacturers they usually exercise a considerable degree of control over the potency and other quality factors and frequently also over advertising claims. The influence of universities administering patents is commonly in the direction of soundness and conservatism.

There is still an additional factor of importance, and this applies not only to university owned patents but also to those which are the property of adequately equipped pharmaceutic houses, and that is the prevention of the improper exploitation of medical products by companies which are not constituted, either scientifically or ethically, to market medical preparations.

It is perhaps unnecessary for me to state that I am convinced of the wisdom of universities, including medical schools, adopting a definite patent policy sufficiently broad in its scope to include the taking of patents by medical members of their staff as well as by others. When I say "definite" I do not mean inflexible because some differentiation I believe needs to be made between discoveries which are entirely the result of the universities' efforts and those which have been made possible by joint work with some one else, such as an affiliate in the pharmaceutic industry.

Various suggestions have been made from time to time of a central repository of research funds and patents. That there is a need for such a central organization for the administration of patents or that it is practically workable, I am not convinced. It seems to me that such an undertaking would be attended with many troublesome complications. Such a bureau might be of interest to a certain number of educational institutions who do not have the machinery, or who do not care to set up the machinery, for the administration of patents. Broad control of university patents by a central body would in my opinion have the effect of pushing industrial and educational institutions apart in their research efforts. The last decade has witnessed a steady growth in cooperation between research workers in universities and colleges and the constantly improving research departments associated with industry. The centralization of university patents would have the effect I am sure of removing much of the incentive toward this type of cooperation and forcing the industrial research laboratories to be competitors instead of co-workers of the investigators located in university centers.

A more constructive step in my opinion would be the formulation of certain general principles which would lead interested schools, including colleges of medicine, to take a positive rather than a negative attitude in the matter of patents and which would lead them to develop a sound patent policy. A broader interest on the part of medical schools in patents would be of great service both to medicine and the public welfare. This does not require any centralization of patents but only a crystallization of sound guiding principles.

DISCUSSION

MR. R. A. NORTON (Calco Chemical Company, Inc.), Bound Brook, N. J.: Mr. Lescohier spoke of the lack of danger of monopolies. That is something which is much in the public eye at the present moment. In dealing with medical patents there are two kinds of monopolies. One is a monopoly which would prevent free distribution or distribution at a reasonable cost to the patient. The other is a monopoly which determines who shall produce. Those two monopolies are different in their effect on human welfare. I don't believe there are any of us here today who would not agree that an abuse of the first monopoly is a very serious thing. A medical patent under no circumstances should be used to keep a remedy from human beings suffering with disease. A monopoly of the second class, which is of the type which is partially affected both by the Scarlet Fever Committee and by the Insulin Committee, and others, determines within limits who is going to manufacture, and that kind of a patent monopoly is not necessarily to be con-

trolled with the same degree of sharpness as the first kind. I got no impression that Mr. Lescohier drew any distinction between those two kinds, and I think a real distinction exists, and one of real importance to social welfare.

DR. AUSTIN A. HAYDEN (Secretary, Board of Trustees, American Medical Association), Chicago: Medical patents are not all necessarily medical. We have been talking about foods, drugs and biologicals. I am interested in another line of patents that comes close to the welfare of the public. I refer to the patents or at least the patented articles that the Council on Physical Therapy has to deal with. In particular I think of the patents that exist on hearing aids and other mechanical contrivances. I believe these are subject to many of the considerations that have been spoken of here this morning in the matter of control, in the matter of the application of their use to the public welfare and, in this particular instance, to the use of handicapped groups of the public.

THE PUBLIC'S STAKE IN THE ADMINISTRATION OF MEDICAL PATENTS

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I should like to beg leave at the outset to change slightly the wording of the topic under which my remarks are to be made. For "the public's stake" I should like to substitute "society's stake." The term "the public" connotes an informed group of persons able and willing to discuss the pros and cons of any problem lying within the field of social policy and social action and which develops, through this discussion, a more or less clearly articulated opinion or consensus. In substituting the term society for the term public I am thus enabled to speak in the interests of those who are neither informed nor articulate about the particular problem under discussion today but who are nevertheless directly affected by the public policies of both private and public agencies no less than their fellows who are more capable of formulating an independent judgment. I assume then the role of spokesman for this larger collectivity.

May I now present what seems to me to be substantial evidence that society does have a stake in and therefore is entitled to the maximum benefits of medical inventions and discoveries. First I would submit the proposition that invention is essentially collective or social rather than individual in nature. This theory denies, of course, Carlyle's "great man" theory of the nature of social change. In support of this social theory of invention, which I feel does not need lengthy elaboration here, I quote Dr. Bernhard J. Stern,[1] outstanding authority in the history of invention. "Medical discoveries and inventions, whether they be in the descriptive field of anatomy, in the diagnosis of causal relations between pathogenic micro-organisms and a specific disease, in the realm of immunology or in surgery and therapeutics have not been made suddenly but have been preceded by a multitude of preliminary and progressive steps which in turn had their antecedents. This principle applies without exception even to those medical discoveries and practices which are popularly considered as the result of the epoch-making work of some individual." Stern cites, by way of illustration, that the contribution of Vesalius was "a combination of humanist intellectual activity and the new naturalist art" for, as Professor Charles Singer has expressed it, "until these two had come together there could be no Vesalius [but] when these two had come together there had to be a Vesalius." The evidence is thus clear that, in the history of medical invention, those who have turned the magic key to unlock doors leading to new medical advance have been indebted to many others who worked to produce the materials for and helped to forge the key itself. This theory does not, of course, deny the importance of the role of the unique individual through whom the invention came to its final formulation. It does however seek to put the inventor in the perspective of his cultural setting. Perhaps the central idea here may be expressed in the dictum that, in the realm of organic life, "all life comes from life"; in the cultural realm the dictum is that "all culture comes from culture." In both cases the doctrine of spontaneous generation is denied. The conclusion then follows that, since medical inventions are essentially cultural rather than individual in origin, they belong to the whole society and through this fact society establishes its claim to their widest and most proper social application.

My second proposition is that the ultimate end of all science is the benefit of mankind. The present confusion on this point is due to the failure to distinguish between pure and applied science. While all science must ultimately justify itself by its contribution to human well-being, each scientist must, in order to do proper scientific work, be motivated only or primarily by a devotion to scientific truth and any considerations which cause him to deviate from striving for that goal are to be rejected as destructive of scientific progress and finally of human progress. Society has then a priceless stake in science and will benefit from it in the measure that the most favorable environment for its development can be assured.

My third proposition is that society has a stake in the maintenance of the proper motivation of research activity, an interest closely related to the problem of the ultimate end of science. It will be helpful, in the elucidation of this proposition, to make a distinction between academic research and industrial research. While the former is concerned with the increase of the body of fundamental knowledge without any immediate thought as to its practical application, the latter is interested in the development, to a practical end, of the fundamental discoveries which the academic laboratories may be expected to furnish. But medical research differs from both of these in the respect that its ultimate aim is the provision of knowledge which will find application in the relief or the prevention of human sickness and suffering.[2] Academic and medical research differ, then, from industrial research in the character of their motivation. The first two, it may be properly said, have a scientific and service orientation respectively, while the third, at least so far as industrial research entrepreneurs are concerned, has an essentially commercial orientation. (I should make it clear that I do not mean to impute base and nonprofessional behavior to the activity or motivation of the industrial research scientist.) It is society's concern that there be no invasion of profit seeking into the first two types of research activity. The survival of a truly scientific tradition depends then on society's insistence that the highest professional standards be maintained in these fields.

Finally, society's stake in medical inventions lies in the generally agreed on proposition that health should not be a commodity dependent for its widest possible distribution and enjoyment solely on the ability to pay a price for it. This is tantamount to the affirmation that health is essentially a public utility. There is suggested here the dichotomy of vendability and serviceability, set forth so ably by Thorstein Veblen in his The Theory of Business Enterprise. Society's concern in the fields of all medical and therapeutic commodities is that the chief desideratum shall be that of their serviceability.

The question may now be raised as to the nature of the present policy or policies which have to do with the patenting or nonpatenting of medical inventions and, in the former case, to the nature of the administration of medical patents. And next, one may ask, What are the consequences for public welfare of the various present arrangements? To a brief consideration of these two questions I should now like to turn.

Concern about the problem of medical inventions, the multiplicity of divergent and in many cases conflicting policies concerning their control or noncontrol, would seem to warrant the conclusion that the present state is one characterized, on the whole, by an absence of uniformity, cooperative endeavor and rational integration. *Laissez faire* or at best a slightly attenuated variety of it would best describe the situation, for there is little evidence of a consistent and clearly formulated professional policy in the matter of the administration of medical inventions and discoveries.

1. Stern, Bernhard, J.: Social Factors in Medical Progress, pp. 100-101, 102.

2. Dale, Sir Henry H.: Academic and Industrial Research, Science **77**, June 2, 1933.

But perhaps the validity of the patenting of medical inventions ought first to be established. Its validity would rest, as I see it, on the simple proposition that in the absence of a patent right there is no legal provision for control, and control would, it seems to me, be particularly indispensable in the field of therapeutic agents. The question is not so much whether medical inventions and discoveries should be patented or not patented but rather it is one concerned with the problem as to whether individual or collective control of these patents would make for the greater public welfare. Finally, on this point I should like to remark that objection to the patenting of medical inventions, either by individuals or by organized groups, on the ground that such action would violate traditional medical ethics would, if the case for its social desirability is established, be confusing means with ends. Efficiency is not, of course, of itself ethical but efficiency as it plays a means role always has ethical effects.

Certain limitations prejudicial to the greatest public welfare appear to attach to the patenting of medical inventions by single individuals. Perhaps of greatest significance among these is the fact that only in the rarest instances would the individual inventor have sufficient resources to defend his patent in the courts. Patents must be policed. This is not a nice fact but unfortunately it is historically true in those instances in which a medical patent was contested for as a medium to monetary profit to the manufacturer. Another limitation which follows from individual patenting is that the formulation of a public policy with respect to the whole problem of patenting and patent administration is thereby rendered all but impossible. Furthermore, the fact that individual control may rest the patent and the rights which it confers with a good and wise person does not, for me, make a totally valid case. Society does need men of good will, but its proper integrity is better guaranteed when men of good will are organized to effect a planned and rational administration of their high purposes. Such a proposition would dictate that the control of medical patents should be vested in institutional rather than in individual hands.

Finally, both the logic and the desirability of institutional control of patents follows from the nature of the process of invention itself. Note that I do not question individual control on the ground that inventors in the field of medical discoveries are prompted by the desire for personal profit. It is all but axiomatic that patents, when they are sought by individuals in this field, are sought for the licensing power to protect society against the exploitation of the fruits of their research.

To invest the universities, in whose laboratories the greater part of scientific medical research is carried on, with the administration of patents would be contrary to my conception of the proper function of the university. It is the custodian of property only so far as it is immediately concerned with the administration of its central function, namely the pursuit of knowledge. As Dr. Morris Fishbein has pointed out in a recent issue of THE JOURNAL, for the university or academic research institute to assume the role of patent administrator might result in changing their tax-free status. The disastrous fiscal consequences alone of such a transition would more than defeat the gains made in the field of patent administration by this method. Dr. Fishbein has also called attention to the fact that such an arrangement might conceivably introduce a harmful competitive element that would certainly not improve the cooperation which has characterized the relationship between academic scientists and which is responsible for much of the progress which scientific inquiry has made.

This extremely sketchy and incomplete statement of the consequences to public welfare of the present practices in the field of medical patent administration brings me to the question of an alternative program. The fact that I have made no reference up to this point to such plans for patent administration as are represented by the Wisconsin Alumni Research Association, the Insulin Committee of the University of Toronto and many others following their general pattern is one of which I am aware. These organizations represent, by and large, the best answer to date to the problem of the administration of medical patents for the general welfare. They combine the merit of constituting institutional rather than individual mechanisms for control and, furthermore, if I understand their organization correctly, they relieve the university administration of extending its efforts into fields not properly its own. Their chief limitation lies, as I see it, in their multiplicity and from that fact in the lack of an integration of their activities. But perhaps even more germane to the problem is the fact that the scope of their operation is limited to medical inventions only in specific institutions and hence does not comprehend the total field of inventive activity in medicine. It is, then, the contribution which the integration of the administration of medical patents could make to science and through it to an expanding public welfare that is, I believe, the paramount need.

While I do not now propose to draw up minute specifications for an organization whose concern with the administration of medical patents would be national in scope, I should like briefly to indicate the function which such an institution might conceivably perform as well as to offer a few suggestions for the general pattern of its structure.

First, such an institution might be conceived merely as a device for integrating the work of the various existing medical institutes, committtes, foundations, university research activities and the like which now undertake to patent and license medical inventions. So conceived, it would serve a function similar to that of the clearing house, providing for such important matters as uniformity of procedure, standardization of patent practice, coordination of research and other relevant activities. In this role it would not disturb the present scheme of patent ownership but would act chiefly in a supervisory and counseling capacity looking toward the most effective administration of the patenting of medical inventions.

A somewhat more comprehensive and ambitious conception would be contained in a proposal to vest in one single national body all the functions now being performed by the existing patent-administering organizations in the field of medical research. Such a plan would of course involve legal complications of the magnitude of which I am quite aware. But whether the national administration of medical patents would follow the first or the second pattern of organization which I have sketched, it would I feel greatly facilitate the progress of medical research and in turn maximize the social benefits from it through a rational administration of medical patents.

Having suggested two general types of organizations for the administration of medical patents on a national scale, I should now like to indicate some of the merits which I feel inhere in this approach to the problem under discussion. The national character of the administrative organization would better equip it to put medical patents to work in the interests of the public welfare in a fashion superior to that which local or regional bodies could do, to say nothing of the superiority of both national and local organizations over the activity of single individuals in this respect. Furthermore the national body could afford an adequate and competent staff of technical, scientific and legal experts, all of whom are indispensable to the proper placing, policing and administration of patents. Its capital resources, created by the method which would seem most feasible and desirable, would be greater and, because of the national scope of the field in which it would be put to work, would be more effective dollar for dollar than the capital of the smaller and scattered organizations which undertake the task of the administration of medical patents. The organization should also be able, because of its larger capital resources, its larger and more expert staff and its national character, to make available data on such problems as manufacturing and marketing, which should be superior to that which the existing patent-administering organizations can furnish. Perhaps more important would be the prospect of its more effective supervision of the conditions under which the inventions under its administration were produced and marketed. In short, it would have all the merits and advantages which a national rather than a local organization has in the administration of a field which is by its nature national rather than local.

As to the question of the staff personnel in such an institution I should feel that its professional make-up would be the function of a reasonable understanding of the nature of its

task. This would dictate that it be composed of persons with the requisite skill and knowledge in the fields of medical therapy and research technics and in the equally important field of institutional administration and management.

While the primary function of such a national organization would be the administration of medical patents, it might properly, though as an item distinctly secondary in importance, perform a useful and presently needed fiscal purpose. It might license patents under a provision which would allow it to participate in a share of the profits of the concerns marketing its patents. Such participation might be sufficient to provide only for the overhead costs of administration. This would permit its organization with considerably smaller capital resources than if it did not share in the profits. But its participation in the manufacturer's profits might be of such a nature as to create additional resources which would be allocated to the member institutions and used by them in the support of their own research activities. In an economy in which the community is facing increasingly heavier tax obligations for the support of basic social services, the amount of tax money available for the subsidy of scientific research may not keep up with the increasing demands for its extension. On the other hand it is not to be denied that the prospect for the continuation of the endowment of scientific research by private gifts could be brighter than it is. Facing such a situation, the provision for research funds through participation by the patent administering organization in the profits from the manufacture of therapeutic commodities may not be entirely beside the point. The allocation of such earnings to research institutions would be made on the basis of the earnings of the inventions which had come from the fruits of their research activity and would be administered through the machinery of these otherwise autonomous member organizations. No prizes or returns would come to individual research workers, and their high professional pride would be the factor which would keep the laboratory free from any suspicion that it had become a party to the commercialization of science. The individual research workers whose labors resulted in a patented invention would have to seek their rewards through professionally adequate salaries and the knowledge that they had made an important contribution to the cause of public health.

In conclusion I should like to say that in the field of public health there must be no such contradiction between production and consumption on the one hand and the rights and duties of the individual and society on the other hand, as there is in certain other fields of endeavor today. The ultimate purpose of such an organization as I have suggested would be to stimulate and guard by rational methods the evolution of the consumptive art for the greatest possible good to both individual and group welfare.

DISCUSSION

MR. CARL S. MINER (Miner Laboratories), Chicago: I have been interested for a good many years in this very problem, not specifically with respect to medical inventions but with respect to university inventions applicable to industry, and I have for the first time heard made publicly what seems to me an adequate suggested solution. Initially, I believe the research foundation of the individual institution was a thoroughly adequate method of handling this problem. Latterly, I have become convinced that that is not the ultimate answer. At least occasionally there is some institution that has a research result that should go into the field of industry and which probably should make some return to the university research funds, but it is all too true that a foundation set up to handle such a single invention might find itself searching for duties to perform at a later date, and perhaps such a situation might result in involuntary pressure being put on the research group of that particular school to produce industrially useful results, which is something to be deplored by all of us. If a national institution were available to which such a relatively small school might take its completed research for exploitation, it would seem that it could answer the question so many of us have been worrying about, and I hope, as one result of this conference today, some group will adequately consider the possibilities of the suggestion Professor Johnson has put before us so ably.

DR. STUART MUDD (Council on Pharmacy and Chemistry, American Medical Association), Philadelphia: I would like to say a word from the point of view of the individual laboratory worker as to how welcome such an institution as Professor Johnson has mentioned would be to us. The present lack of any policy, or any ethic, really, to guide us when we have something that we feel is useful, or anybody in our own institution whose responsibility it is to advise us and take hold of anything worth while and do the constructive thing with it, is a very serious matter. We are floundering. We don't know what to do. If we had some institution of this sort that we could trust, that could advise us wisely and take hold of the things that are developed in the laboratories and use them ethically and for the good of science, and bring some return for the subsidizing of scientific research, it would be the greatest comfort to the research worker. I think I can say that with a great deal of assurance.

DR. R. E. DYER (U. S. Public Health Service), Washington, D. C.: In the discussion so far there are some things that stand out somewhat clearly, and one of them is the possible difference in attitude of a government agency, or an institution that is supported by tax funds, in comparison to a manufacturing establishment or to an individual. It seems reasonably clear that the policy Dr. Long outlined this morning as one in process of development for the National Research Council might apply to one set of institutions or to one group of men, but not be at all applicable to another group. It brings out the difficulty of establishing any general policy to handle all particular questions. Something along the line that Professor Johnson has just suggested may prove a satisfactory solution, in that such a body could be empowered to handle each individual question on its merits, determine the patentability of a discovery, the remuneration of the discoverer and the implementation of the patent for the benefit of the public.

DR. MORRIS FISHBEIN (Editor, THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION), Chicago: The fact that such discussions are continuing before this organization, before the National Research Council, before the American Chemical Society and before many other groups should indicate that the present situation is not satisfactory. The fact that there are constant allusions to interference with research in universities, in state health departments and other places would indicate that probably from time to time there has been interference with research. The fact that time and again universities have been accused of being interested primarily in the amount of income to be derived from patents rather than in basic research would indicate that at least a considerable number of people have the view that such an interest is occasionally manifest. Obviously, discussions will go on until some satisfactory solution is found of the problem of administering medical patents primarily for the public welfare. That duty we owe to society, particularly in relationship to the prevention of suffering and the control and treatment of disease. I do not know the answer to this question any more than any one else knows it. If an answer is to be found, aside from government control and administration, it must be found in some voluntary activity in which all of those who are concerned, including the individual physician, the university, the manufacturer and all other groups concerned, will come together and work out a mutually satisfactory solution which protects the rights of the inventor, the manufacturer and the university and which at the same time keeps primarily in mind the rights of the patient and of the public. Such a voluntary agency must be formed on a national scale, with sufficient strength and force to be able to administer such patents for the good of all. The suggestion made by Professor Johnson does not appear to be sufficiently worked out in detail to satisfy every one, but sooner or later it will be necessary to establish some such body. The fact that the National Research Council has seen the desirability of a corporation for the administration of such patents as come under its control would indicate their belief that an organization of that type is necessary. We are not here to adopt today any definite conclusions. We are merely here to study a trend. To me it seems that the trend is going to be toward the formation of a national organization for the administration of medical patents in the public interest.

DR. J. C. MORRELL (Universal Oil Products Company), Chicago: As I understood Mr. Johnson's thesis, it takes care of the administration of the patent so far as the public is concerned. I didn't quite understand how the individual inventor fits into this picture. The last thing I got was that, preferably, he should be a salaried employee. I am sure that such salaried employees of an organization of that kind would make only a small percentage of the contributions to medical science and that Mr. Johnson's proposal is not a general solution of the problem from this point of view. I would like to ask Mr. Johnson just how the individual inventor will be taken care of by the method which he suggests.

DR. ESMOND R. LONG, Washington, D. C.: I rise merely to make a minor correction in Dr. Fishbein's remarks. I believe the Research Council would welcome an organization in which we all had thorough confidence to take care of the difficult problems that come before us. As I mentioned this morning, we are exploring the possibilities with such an organization. The one I mentioned is not organized for operation on the scale necessary for such a task as Professor Johnson has visualized but has made definite progress in that direction. I am presenting no special brief for this organization. It has been useful to us for certain substances; you will recall, however, that the Council's resolutions which I read to you stated specifically that the council could take advantage of this organization or any other set up for a similar purpose. The organization to which I refer is the Research Corporation of New York.

DR. ROGER I. LEE (Harvard Corporation), Boston: At Harvard University we have had a good deal of experience, as have all universities, with regard to these perplexing patents. In the first instance, to be specific, we had the so-called Drinker patent, the Drinker respirator, which was devised by Mr. Phillip Drinker, who was a member of the School of Public Health and not a doctor. That was patented and led to a great deal of grief on the part of all concerned, including the Drinkers, the holders of the patents and various other people. The next important step in our history was the formation of a Committee on Anemia to take charge of the work of Minot, Murphy and others with regard to the so-called cure of pernicious anemia. That committee of the Harvard Medical School operated, not entirely satisfactorily perhaps, but still it operated without a patent and, on the whole, the advantages seemed far to outweigh the disadvantages. The university has scrutinized with a great deal of care all the pros and cons and, without repeating the arguments one way or another, and particularly with the utmost friendliness for industry, because it feels that the university should not go into active competition with industry. If the university, in its position, goes into active competition with industry it is unfair competition, it seemed to us, with a good many advantages on the part of the university. Finally the university made the following ruling. I go back to May 28, 1934. The president of the university communicated to the Corporation the following votes of the faculties: "In the opinion of the Faculties of Medicine, Public Health, Engineering and Arts and Sciences of Harvard University, the patenting by members of the university of discoveries or inventions bearing on matters of health and therapeutics is undesirable." Those were separate votes of each of those different faculties. These several faculties recommend that the president and Fellows of Harvard College adopt the following rule: "That no patents primarily concerned with therapeutics or public health may be taken out by any member of the university, except with the consent of the president and Fellows, nor will such patents be taken out by the university itself unless they be dedicated to the public. The president and Fellows will provide legal advice to any one who desires steps to be taken to prevent the patenting by others of his discoveries or inventions." It was voted to adopt this rule and that the policy of the university with regard to patents is given in the following statement: "In the opinion of the Faculties of Medicine, Public Health, Engineering and Arts and Sciences, the patenting by members of the university of discoveries or inventions bearing on matters of health and therapeutics is undesirable. The president and Fellows of Harvard College, therefore, have adopted the rule that no patents primarily concerned with therapeutics or public health may be taken out by any member of the university, except with the consent of the president and Fellows, nor will such patents be taken out by the university itself unless they be dedicated to the public. The president and Fellows will provide legal advice to any one who desires steps to be taken to prevent the patenting by others of his discoveries or inventions." Then a year later, May 20, 1935, it was voted to adopt the following statement for the guidance of members of the university in matters relating to discoveries or inventions primarily concerned with public health and therapeutics: "In connection with the policy of the university to make available to the public discoveries or inventions primarily concerned with public health and therapeutics, there is evidence that in some cases it may be necessary to take out a patent and dedicate it to the public in order to prevent others from obtaining a patent for their own benefit. Accordingly each member of the university is asked to report any such discovery or invention made by him to the dean of his faculty, with a recommendation as to whether it should be patented for the above purpose, in order that if necessary steps may be taken to obtain and dedicate the patent. If the member making any such discovery or invention believes it should be patented for any other reason, he should so report to the dean, giving his reasons in full so that the matter may be submitted to the Corporation for decision."

DR. H. L. RUSSELL (Wisconsin Alumni Research Foundation), Madison, Wis.: I don't think, Mr. Chairman, there is anything I can contribute, representing the Wisconsin Alumni Research Foundation. I believe the principles laid down by Professor Johnson have merit and, from the point of view of unifying and integrating work of this character, something of that sort might be worked out. That probably will not become effective immediately and, in the meantime, the several foundations that are interested in matters of this sort probably will continue to function, I presume.

DR. JAMES M. NEILL (Cornell University), New York: In all discussions on methods of administration of patents, it is well to remember that the opinion in this country is not unanimous that it is either desirable or necessary to take medical patents at all. To me there seems to be only one argument to indicate that patenting by universities or endowed hospitals would ever be desirable; that is, the possibility that discoveries made there might subsequently be patented by other people. If that one objection could be removed (and perhaps the danger from that source is overemphasized), I believe there would be no question that all schools and hospitals would gain more than they would lose by the simple rule that they do not patent anything under any circumstances. At any event, I think the setting up of a large central body like that proposed by Professor Johnson would be a bad thing to do because the existence of a board of that sort would be more likely to increase than to decrease the present tendency toward too many patents.

MR. EARL S. JOHNSON: If I understood the gentleman correctly, his question had to do with what provision this institution, which I have sketched in very brief outline—what service it would perform for the lone wolf.

DR. MORRELL: Both the lone wolf and the individual working in some institution outside of this proposed national institution.

MR. JOHNSON: I should think the member bodies of the national institution would be various types of research organizations. They might be research institutes; they might be the university laboratories themselves. With reference to the lone wolf inventor, I thought he had generally gone west with the buffalo. I may be misinformed about that. I think he is of relatively little significance, although his contributions may be very important, still. As I read the history of social change, I see increasing institutionalization of the whole process of invention. I should, of course, want to take account of these rare birds who are still about and would offer them under some definite prescription the opportunity for their researches being piped into this organization to get from it the kind of services it could render. I have only this other thing to say, Dr. Lee, that either I have made a very startling remark, which

is profound in its significance and is so brilliant and intelligent that you gentlemen, who are both profound and intelligent, have seen the wisdom of it; or it is a very ordinary and naive one which is as old as the hills, and I go back to my colleagues heartened and warmed and to say that under some circumstances even what a sociologist says makes common sense.

MEDICAL PATENTS AND THE LICENSING SYSTEM FROM THE POINT OF VIEW OF THE COUNCIL ON PHARMACY AND CHEMISTRY

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The Council on Pharmacy and Chemistry does not have fixed views on this subject. I give you my interpretation of what I think the Council views are as I have heard them expressed at various times.

The Council has an open mind on the subject of patents. It realizes, as you all do, that this is an extremely complex problem that at present, I think, is not amenable to a very simple solution. We may hope to work toward one by experimentation along some of the lines that have been discussed, and I think perhaps, in the end, we shall arrive at something that is fairly workable, but it is perhaps lucky for us that we do not have to come to a decision today.

The Council on Pharmacy and Chemistry has for its function the advising of the American Medical Association regarding new drugs offered for prescribing by physicians. Being new, the drugs often are patented. That fact is taken for granted by the Council, especially as it applies to manufacturing houses.

I think all of us, when we think about the subject with a little knowledge, realize that the introduction of a new substance by a manufacturing house is an expensive and a risky process which, in general, could not be undertaken unless there was some degree of monopoly granted. Recognizing that as applying to manufacturing houses, the Council also has to recognize it as applying to other individuals. We have to accept the fact that patents are taken out by universities and are taken out by individuals.

It does seem to me, however, that universities do have a special obligation to the public in view of the way in which they are supported by the public, and that the members of universities have obligations both to the public and to the universities, because the very fact that they can work at all is due to the universities and to the public. Therefore they are not entirely, to my mind at least, in the free position, as regards taking out monopolies, that exists for manufacturing houses. Manufacturing houses need to consider in this respect, I think, only whether the thing is good policy. In the case of the universities they have to go a little further and have to consider whether it is fair to the conditions under which they exist.

While the Council does not combat patents as such, it has been in position to observe perhaps more clearly than some others that there are tendencies in patenting that are unfortunate. I think that most of those have already been brought out but I do wish to discuss them a little more. They are unfortunate for the manufacturing houses, and very much more unfortunate in the case of universities.

The whole matter, I think, begins with the Patent Office. After all, when patents were instituted it was not medical inventions that were in the minds of Congress but particularly mechanical inventions of various kinds. The whole Patent Office is set up for that and not for medical patents, and considerable difficulties arise from that, from a want of understanding, for one thing, of what is involved in medical patents, and also from want of understanding that the situations are not entirely comparable. The Patent Office is geared to the industries and not to the practice of medicine.

The patent laws were instituted, as we have been told, to promote useful inventions. Notwithstanding what has been said, I think it is on the whole questionable whether they have promoted very greatly invention in medicine, and especially in universities. I believe all the inventions in medicine that have been made, that are worth anything at all, would have been made just the same and at just about the same time if there had been no patents in existence and no patent protection. They might not have been popularized so fast, but that is another story. But as to invention, I do not believe they have had much influence.

Again, the intent of the patents was to promote the disclosure of secrets and again I doubt whether any material secret in regard to medical matters has been disclosed because a patent could be obtained on them. I think they would have been disclosed, if they had been invented, in just the same way as they were disclosed under the patent.

Then, again, in order to be patented the invention should be new and it should be useful. As Professor Johnson has very well brought out, when we delve into the newness of the things on which patents are issued a great number of these inventions are simply putting a capstone on what other people have done, and with very unequal justice. It happens not infrequently that the people who have done the fundamental work have been the kind who did not care to take out patents, and then some one comes along and adds just a little to it and takes out a patent.

On the matter of usefulness, a medical invention is not useful until it has been tried out by unprejudiced clinicians and pharmacologists. As soon as you have a monopoly there is, in the first place, a tendency to have a prejudice and, in the second place, the secrecy that is demanded before a patent is obtained works against getting a wide experience with the substance. It works in just the way in which it is not intended to work.

It has been mentioned to us that patenting by universities instead of aiding invention tends to prevent it, that it interferes in ways sometimes intended, perhaps more often not intended, with other people working at the subject. It tends to keep matters secret until the patent is obtained which, if known, would give some one else an idea to advance further.

There is a particularly objectionable type of patenting, as I see it, that consists in patenting the mixing of well known drugs, with the claim that a new action is obtained. Very often those drugs exist together in nature, have always been used together—unintentionally, it may be—but it does seem to me that nothing is furthered by patenting what nature has provided without a patent. On the other hand, as soon as you patent the prescribing together of things you interfere seriously with what should be the privilege of the physician, that of prescribing things together as he may wish to prescribe them. He may not want to prescribe forms that the manufacturer puts up, but as soon as a patent is obtained on mixing things he cannot go further.

The argument that is made for financing further research by patents has very serious drawbacks. Of course, we all understand that the support of research in universities is diminishing, and we may have to wait some time until another way of financing is found. But as soon as we introduce a profit motive, whether it be for the individual or whether it be for the university, we introduce a motive that, it seems to me, kills off a good deal of that for which the universities have stood and are standing. Research in universities should be free from money motives. As soon as the money motive enters—whether it is for the support of further research or the football team, makes no essential difference—the university laboratory becomes a commercial laboratory, usually not as well organized for commercial research as commercial houses can organize it. It is apt to be a second-rate commercial laboratory.

I think if there is any justification—and we all know there is—for university research, it is that the profit motive is kept away from it, so that it can go after fundamental things which other people do not feel as free to go for. If this is the only way in which universities can be saved, that is, by making money out of research, then it becomes a grave question as to whether they are being saved as universities or are not being made into something else, something that may not be worth saving.

Now comes the argument of control of abuses, and that has a good many very telling points which make it a subject on which I, for one, am not ready to decide. They have all been brought up, many of them at least: the matter of piracy, the matter of preventing low standards, and so on.

I think Professor Johnson is on the right track there: if the universities patent things to protect the public, it would be better to give the profit to somebody else and so be quite sure of their motive.

Another argument is that without this protection it would not pay any one to market the invention even though it would be free to manufacture. We do have some outstanding examples on the other side. The antianemic principle of liver certainly went across without patenting; so did sulfanilamide. If something is really good enough there is no need to promote it by a patent or to protect it by a patent. The laws as they now stand would be sufficient for that. Of course, there are many things not quite big enough for that, and for them protection may be useful or necessary.

There is a related topic, not a patent but something that takes the place of it, the copyrighted name or trade-mark, which has not been mentioned. This device seems to defeat or at least evade the intent of the patent, of protecting a monopoly for a short time, by substituting an indefinitely prolonged protection. There may be cases for which seven years or fourteen years—whatever the time may be that a patent can be made to run by subsidiary patents, or what-not—may not be sufficient. It is quite possible, but it does seem too bad that it is necessary to evade a law in order to make it work. It would seem much better to legislate needed extensions of the patent rather than to go around the corner and try to accomplish the same thing in an entirely different way.

All these matters could be improved, no doubt, by improving the laws. As has been mentioned, perhaps the patent law as a whole should be improved. It may be, as Mr. Hutchison mentioned, that there should be a special modification of the patent law applicable to drugs and devices, because they do have a special relation. Perhaps it would be well if the Patent Office had a special machinery for doing this and did not throw it over to people whose knowledge of medical matters is apparently not very great. I think probably more can be accomplished by the way in which the patent laws are applied and interpreted than has as yet been done. I think things are setting in that direction.

The financial reward of the inventor is not a direct concern of the Council but it is difficult to dissociate these matters. I think it would be very unfortunate if in universities there should be professors who make a large amount of money or indeed, any amount of money because they devote themselves to inventions, as opposed to another class who are equally able and who devote themselves to the proper business of the university. You have here the professor of mathematics, perhaps, who has no opportunity of making inventions, as against the professor of, let us say, pharmacology, who might have considerable opportunity for an income from patents. When you introduce the profit motive into universities, things go askew.

The views which I have expressed, while they may be shared by the other members of the Council, are largely personal. The Council does not control the law of the land; it has to work under the law and with it. It can, however, and does have its own standards, which are not necessarily the same as those of the Patent Office. And knowing, as I think it does, the problems of medicine and therapeutics more intimately, it should take some leadership toward improving the attitudes that pertain to medical patents.

Coming to the practical things, I think the measure our chairman has outlined as having been taken by Harvard is good. It sets up a presumption that one should avoid patents unless they are necessary. It sets up a machinery by which a disinterested body determines whether they are necessary or not, and it directly specifies that those who are concerned in taking out the patent, be it as individuals or as an institution, shall not have a profit motive in taking them out. Whether, beyond that, it is advisable to go to a national organization such as Professor Johnson outlined is an interesting speculation at this moment, which holds a great deal of promise. It is nothing new, as the National Research Council has pointed out. There is even now an organization to which such patents could be turned over, but it is not primarily concerned with medical patents and for the reason with which I started, namely that medical and nonmedical patents are rather distinct things. I think, if one went ahead with this, it would be advisable to have a separate organization for medical patents.

DISCUSSION

DR. EUGENE F. DU BOIS (Professor of Medicine, Cornell University), New York: The minority point of view, it seems to me, is being brought out in this latter part of the discussion —such a view as that of the National Research Council, of Harvard University, of my colleague Dr. Neill, of Dr. Fishbein and of Dr. Sollmann. I can see how it is necessary for a university to take out patents in certain rare cases, very much as a nation might have to set up a defensive armament made necessary by the aggressive armaments of others, but in my opinion such patenting should not be used for the acquisition of new territory, no matter how fertile and desirable it might seem. I should like to emphasize an intangible subject, reputation, the most precious possession of any university, the only thing that really counts. It is quite conceivable that a university, in using a patent to get new funds for research work, might gain a few thousand dollars. It also might lose millions, not millions in dollars but millions in some other unit that measures reputation. The same thing might apply to the individual. Reputation is just as important to the individual as it is to the university, and if a man utilized the large amount of fundamental work that had been accomplished by others in his field and took out a patent he would be in danger of suppressing fundamental work done by his colleagues and he might not allot proper credit. He would be in danger of losing the one great attribute of the research worker; that is, his reputation for fundamental work in his own field.

MR. R. A. NORTON (Calco Chemical Company, Inc.), Bound Brook, N. J.: I merely wanted to make a brief statement amplifying the proposition that Dr. Sollmann has put up, that medical patents should be treated in a different manner from ordinary chemical or mechanical patents. Dr. Sollmann's statement, I am afraid, leaves the impression that that is not being done at the present time. I can state from my own personal knowledge, some of it painful, that it is. There is a very definite, fixed rule in the Patent Office today that the degree of invention required in a medical patent is of an entirely different order of magnitude from that required to support a mechanical patent. This last month a patent was granted, which I prosecuted, in which I had the greatest difficulty in persuading the Patent Office that the clinical evidence which satisfied the Council of the American Medical Association was sufficient evidence that the product was useful and not harmful, and it was only after extended argument that I convinced the examiner. Its standards today are high. It is handicapped only to the extent that it must deal with evidence which is submitted ex parte in the form of affidavits and is therefore vulnerable to any evidence which is not sincere. But that type of evidence is not as easy to get as it used to be. At present, that is a rule of the Patent Office, merely by commissioner's order and not by statute. Conceivably it might be changed. I don't believe it should be changed. If it is necessary in any one's opinion to have a statutory provision to keep this high standard, I think that would be one that few of us would have any objection to. With regard to the question of mixtures of drugs, to which Dr. Sollmann has referred, there is a very definite trend in the Patent Office today to refuse a patent on any mixture unless it can be shown conclusively—and it requires very severe evidence—that the combined result of the two drugs is more than the sum of their individual results and is a result which could not be predicted and would not be expected. I think, therefore, that the provisions Dr. Sollmann feels are necessary in order to protect medical patents are, to a very large measure, already in existence in the Patent Office, and I hope, for one, that the Patent Office keeps up the good work.

DR. F. W. SULLIVAN JR. (American Chemical Society), Washington, D. C.: The American Chemical Society appreciates very much the opportunity to be represented at this conference. Our society is actively interested in patent affairs and is cooperating through one of the members of its Patent Committee with the National Advisory Council to the House Committee on Patents. I am sure that our society will be very glad to continue its association with other meetings of this sort sponsored by your organization.

DR. ELMER L. SEVRINGHAUS (Professor of Medicine, University of Wisconsin Medical School), Madison, Wis.: It is obvious that much of our conclusion must be based on generalizations, and yet I think we were helped, especially this morning, by the concrete cases that were discussed, particularly with the scarlet fever and the insulin work. The one alternative to the patenting that has been mentioned seriously is the experience of the Harvard University group that the chairman has mentioned to us. I wonder, however, whether it would be out of order to ask that we have some further details about how that has worked out in the matter of control, the prevention of exploitation, and particularly in the uniformity of product —the product control. That is not a question that bears on only the antianemic material but I think, by analogy, has a great deal to do with the situation in the endocrine field, which is rapidly becoming chaotic because of the diversity of products, the different kinds of units, and so on. If this method of control without patent can operate to insure good product uniformity, I think it might help us in our thinking to know how it works.

CHAIRMAN LEE: If I may very informally answer that question as far as I can, of course there has been no attempt to control the antianemic factor. That has been thrown open to the public. The committee has simply advised in the progress of the work at the university. It has been willing to advise and to give all possible assistance and immediate data to any of the industrial houses that wanted it. There has been no attempt in this instance to exercise any control. It is the opinion of people who are close to the work that, on the whole, it has worked satisfactorily; that, on the whole, it has worked well with less hardship than would have occurred probably if it had been patented. It has resulted, as we all know, in great and active research on the part of many workers and many of the industrial concerns. Out of that has come, as by-products, a great deal of important data, some of which are very much more important than the actual preliminary liver work, and the work on the liver fraction which at that time was thought to be the underlying factor in the cure and control of pernicious anemia. Some of the work has been done in the Harvard Medical School but a great deal of it has been done elsewhere, and it has seemed to some of us that it was important that it should be done elsewhere because, after all, the work on the liver business was probably started in a great many places—probably not at Harvard University, although they happened on the real factor, which was the size of the dose of liver. Given a few months more, undoubtedly that would have happened somewhere else, and I am under the impression that it did happen in other places at about the same time that it happened at Harvard University. But there has been, I think, in the antianemic factor a tremendous amount of research activity and it seems to me doubtful—while this is just an opinion, nobody can prove it one way or another—that the same amount of research activity would have happened under any other situation.

DR. J. C. MORRELL, Chicago: I am going to risk getting up again on what I consider a rather important point, which is a technical question from the patent point of view, and that is if a university or other organization or even an individual wants to make discoveries for beneficent purposes without gain to itself and dedicates a patent, for example, to the public, this procedure may have undesirable results in that it permits a group of secondary inventors to come in and perhaps control the use of the product to the detriment of the public. I will cite an example: Take the case of sulfanilamide. If sulfanilamide had been patented and was not dedicated to the public for its free use because of the prior art it could be controlled by a beneficent organization, which could permit its proper distribution and use without charge, if desired, by those groups or individuals who are qualified and should be entitled to distribute it. The use of the diethylene glycol as a solvent for sulfanilamide could not have been as widespread, with the dire results which followed, because it would have been dominated by the main patent; and the distributor would have been subject to suit for infringement. I think that is a point which is well worth noting, that merely dedicating a patent to the public will not protect the public, but the product should be patented and kept under some control to prevent these secondary developments and patents which may control the situation if the dominating or protecting influence of the primary patent is not present or has been removed.

MR. F. LORNE HUTCHISON, Toronto: I gather that Dr. Sollmann is not just quite sure in his own mind as to the extent to which the public interest needs protection through patenting. I think he is quite right; I don't believe this need is particularly frequent. Moreover, I think the United States is probably somewhat alone in the matter of possibilities of patent piracy. But I do want to give Dr. Sollmann one actual example of need that was demonstrated for patenting in the public interest: In 1922 insulin was first used clinically. There was no desire whatever on the part of Banting and Best, their colleagues or the University of Toronto to take a patent on insulin. Furthermore, we had not heard of patent pirates because under our law patent piracy is, I think, not possible, although of that I am not sure. But it was brought home to Banting and Best and their colleagues that, though insulin was only in the initial stages of its development and had not been perfected for clinical use, it was obvious not only that there would be great and urgent demand for the product but also that some material improvement in the product would probably be made quite soon, which improvement might be made outside the university by some party actuated by profit motives who might obtain a patent that could be administered purely for his own benefit or the benefit of his company, were the University of Toronto not to obtain a basic patent to which improvement patents would be subsidiary. Fear of the dangers of such a development proved within a few months to have been warranted. A material improvement in the process of preparing insulin was discovered. As this improved process was patentable, it could have developed that the whole world would have had to pay excessive tribute to the inventor of this process had there not been a basic patent standing in the way, and had our necks not been saved by a happy combination of other fortunate circumstances. It was only in these circumstances that it proved possible to avoid dangers which were originally feared and which easily might have actually materialized within a year of the first clinical use of insulin. I also agree with Dr. Du Bois that such instances are rare. As you can imagine, in the years following 1922 there were plenty of patentable discoveries made at the University of Toronto. It was not, however, until twelve years later that another patent was taken by the university. Whereas the insulin patent had two *raisons d'être*, namely protection and control, this second patent was taken only for purposes of protection. It related to a machine which at that time looked valuable for use in reducing and preventing the incidence of silicosis in mines. Obviously, this machine might readily have been improved by some one who might take a patent on the improvement and collect excessive royalties from it. The university in these circumstances was advised that, as there might be a demand for this machine in all countries where there were gold mines, a patent should be taken in order to prevent any one from levying excessive tribute from either slight or material improvement of the machine. A basic patent was therefore obtained for dedication to the public through the offices of the Ontario Mining Association, which was willing to make rights to its use free to any proper person in the world who wished to use it.

DR. TORALD SOLLMANN, Cleveland: I quite agree with Dr. Du Bois and Mr. Hutchison that there are occasions when patents for the protection of the public are advisable; but, when the profit motive enters, those occasions undoubtedly seem more numerous than without the profit.

ADDRESS OF SENATOR ROBERT A. TAFT

AT LAYING OF CORNER-STONE OF DOCTORS' BUILDING, WASHINGTON, D. C., JULY 11

It gives me the greatest pleasure to say a few words at the laying of the corner-stone of the Doctors' Hospital here in Washington. Almost unique among similar enterprises of the present day, this building is being constructed entirely from private resources, without government assistance of any kind whatsoever. It is designed to provide 250 additional hospital beds for the District of Columbia, of a simple but efficient character, designed to reach patients who can pay approximately $6 a day either from their own resources or as members of the hospital associations, which have been extended so widely in the District. It has been organized, and the money raised by doctors, to meet the local need for hospitals, in a city which is perhaps growing faster than any other city in the United States because of the increased activities of the government departments. I enjoy the opportunity of praising the initiative of the medical profession of the District in working out its own problems without lying down on the government.

To some extent the medical profession is subject to the same criticism which is often directed at members of the legal profession. The abler members of the profession are likely to become so busy in their own practice that they pay too little attention to the question whether the profession as a whole is covering adequately its whole broad field of public service. Because their own task is well done, they are likely to feel no great concern about the question whether the administration of law or the administration of medicine is serving the public and the country as it should. Of course this is only a generalization, for countless reforms in the field of law have been initiated by lawyers, and countless reforms in the field of medicine by doctors. Here today we see how constructive enterprises are carried through to success if a few men are willing to devote their time and energy to the task.

We have before us in Congress today the National Health Bill introduced by Senator Wagner, proposing to extend vast federal assistance throughout the field of public health and medical care. It appropriates, out of our growing deficit, approximately $100,000,000 of federal money the first year, and gradually increasing sums thereafter, until in ten years it will cost the federal government more than $400,000,000 and require the states to supply approximately the same amount. This money is to be distributed to those states which have adopted state plans in various fields of medical work. In general the character of the plan is left to the state, but the appropriation of money collected from all the states to those states which go along with the program forces all the states as a practical matter to adopt some plan in each one of the fields covered by the bill. Six categories of state activity are provided for, namely maternal and child welfare, handicapped children, public health work, hospitals, general medical care and sickness insurance. The bill has been strenuously attacked by many witnesses from the medical profession and is not likely to be pressed at this session, but I believe that in 1940 a federal medical program of some kind will be adopted. What form it takes depends largely on the medical profession. I am most hopeful that the doctors determine what comprehensive program can be adopted to improve the health of the American people, and that they propose a practical measure to assist that program.

The present bill seems to me needlessly complicated. Its administration will take place under three different federal departments. Every state must adopt at least six separate plans, and for each plan there is an advisory committee, so that the bill will create approximately 300 different boards, largely composed of laymen. Surely the federal health program ought to be consolidated under one head, and each state program ought to be worked out as far as possible under a single state department. The doctors feel very strongly, and I think justifiably, that, while the Wagner bill does not itself contain specifically a program of socialized medicine, it is proposed by those who favor socialized medicine and is open to the suspicion that it will afford a vehicle through which they may put their state-controlled medical care into effect. I feel confident that proper amendment of the bill can prevent such a result. We should be, above all, concerned that every patient retain the right to select his own physician, so that the personal relationship may not be disturbed and the success of the individual physician may depend on his real ability instead of his political connections. We should be concerned that no great proportion of the doctors ever become employees of government. I see no reason why the present condition of individual service should not be preserved, even though we adopt the principle of federal financial assistance.

Undoubtedly the deficiency in medical service in many parts of the United States has been exaggerated in the report of the sponsors of the bill, but nevertheless there is a lack of such service, resulting principally from the poverty of millions of American citizens. Unable to pay for medical service, they find no service at all in some rural sections or they find the free service supplied by their cities or states inadequate or ineffective, and they may not be fortunate enough to receive any of the tremendous amount of charitable service provided by physicians themselves. Of course nothing is more important than health in meeting the problems of the average family and, if possible, it is even more important to those unable to pay for assistance than it is for those who are better off financially.

There are those who question the wisdom of any federal assistance in the health field, but, as in the case of relief and old age pensions, we have found that the states and localities have practically exhausted their financial resources in dealing with the established activities of government, like schools, roads and city services. They were unable to push on into the new field of assisting those classes who receive inadequate income, through relief and old age pensions. Most localities and states have undertaken health work but do not have the funds to make it universally effective. Some localities have never been able to undertake it at all. Assistance from the federal government in some fields is essential, and such assistance seems to me justified in the field of public health, provided it is in a reasonable amount to meet real needs in a sensible and economic manner.

The sponsors of the present bill seem to exaggerate grossly the lack of hospital service in the United States. Disregarding all private hospital service, they apparently plan a vast system of public hospitals to take care of everybody who would like to go to a free hospital. Any hospital plan should certainly encourage the construction of private hospitals and their use by public and private patients to their full capacity. It should encourage private plans of hospital insurance, which will assist the success of private hospitals and reduce the expense of operating public hospitals. The construction of this Doctors' Hospital here in Washington shows that a large part of our problem may be met without the pouring out of more millions from the federal treasury and without turning over to some state or federal official the entire determination of who shall receive hospitalization and when he shall receive it; and the hospital plan ought to be worked out deliberately to encourage philanthropic persons to invest their own money in the extension of private hospital service, as they have so liberally invested it during the past fifty years.

There is hardly a field in which there has been more sensational and continuous improvement than that of medicine in the United States. That improvement has been due to the brilliant, unselfish and industrious work of thousands of physicians. It is not their fault that incomes are unequally distributed and that efforts by local government to cover the entire field of health have been restricted by lack of resources. But now I hope they will take an active interest in seeing that the unequaled medical service received by most Americans is extended to the entire population. Their own interest and participation in the program will make it certain that it is not dominated by half-baked theorists or by those who believe in a totalitarian state, directing the lives and caring for the health of all its citizens through the mechanical and usually careless action of government bureaus. I believe a federal aid program can be worked out. I believe it can be much simpler and much more economical, and much more likely to preserve the essential independence of the doctors than the present Wagner bill. I believe it can be worked out with the assistance and cooperation of the doctors themselves.

MEDICAL LEGISLATION

DISTRICT OF COLUMBIA

Changes in Status.—H. R. 4732 and H. R. 4733 have been reported to the House with amendments, providing respectively for the issuance of a license to practice chiropractic in the District of Columbia to George M. Corriveau and Laura T. Corriveau. H. R. 6266 has been reported to the House, providing for the incorporation of certain persons as Group Hospitalization, Inc., the corporation to be authorized to enter into contracts with individuals or groups of individuals to provide for hospitalization of such individuals, to enter into contracts with hospitals for the care and treatment of such individuals, and to cooperate, consolidate or contract with groups or organizations interested in promoting and safeguarding the public health.

MEDICAL BILLS IN CONGRESS

Changes in Status.—The President has vetoed H. R. 3537, proposing to extend the facilities of the United States Public Health Service to active officers of the foreign service of the United States. The bill, the President said in his veto message, would open up a wholly new field of government medical and dental care for government servants and to establish such a government policy would in a short time involve "setting up of dispensaries and bed facilities in every place in the country where there are many employees of the government" (S. Doc. 431). S. 1540 has been reported to the House, proposing to increase the compensation of members of the National Advisory Health Council not in the regular employment of the government. S. 1899 has been reported to the House, providing for the detail of a commissioned medical officer of the Public Health Service to serve as assistant to the Surgeon General. S. 2420 has been reported to the Senate, proposing to authorize the Secretary of the Interior to cause to be made annual inspections and investigations in coal mines for the purpose of obtaining information relating to health and safety conditions, accidents and occupational diseases therein. H. R. 6076 has passed the Senate, providing for the registry of surgeons as staff officers on vessels of the United States. H. R. 6555 has passed the House, proposing to amend the law relating to the advance of funds in connection with the enforcement of acts relating to narcotic drugs, so as to permit such advances in connection with the enforcement of the Marihuana Tax Act of 1937. H. R. 6556 has passed the House, providing for the seizure and forfeiture of vessels, vehicles and aircraft used to transport narcotic drugs, firearms and counterfeit coins, obligations, securities and paraphernalia.

Bills Introduced.—Senate 2802, introduced by Senator Sheppard, Texas, proposes to amend an act authorizing the operation of stands in federal buildings by blind persons. Under the present law a blind person is defined to mean a person having not more than 10 per cent of visual acuity in the better eye with correction. Such blindness must be certified by a duly licensed ophthalmologist. The pending bill proposes to define a blind person as a person having not more than 20/200 of visual acuity in the better eye with maximum correction or a person whose field of vision is limited to 20 degrees or less from the fixation point in all quadrants. The pending bill eliminates the requirement that the blindness must be certified to by a duly licensed ophthalmologist. Senate 2862, introduced by Senator Wagner, New York, proposes to provide compensation for disability or death resulting from injury to employees of interstate carriers. The bill devolves on employers the duty to furnish such medical, surgical and other attendance or treatment, nurse and hospital service, medicine, crutches and apparatus for such period as the nature of the injury or the process of recovery may require. The term "injury" is defined to mean "accidental or wilfully caused injury or death arising out of and in the course of employment, and such disease or infection as naturally or unavoidably results from such accidental injury, and such disease or infection as arises out of employment." H. R. 7243, introduced by Representative Starnes, Alabama, proposes to make appropriations for public works projects. It provides that not to exceed $50,000,000 shall be allotted to federal agencies for federal construction projects, to include specifically projects for hospital and domiciliary facilities of the Veterans' Administration and projects for hospital, quarantine and laboratory facilities under the Public Health Service in the Federal Security Agency. Other funds are to be utilized, it is proposed, in making loans or grants to public agencies and to nonprofit corporations for the construction, improvement or extension of hospital facilities, for sewage treatment or disposal plants and for the elimination of pollution in streams.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Fund for Study of Respiratory Diseases. — Mr. and Mrs. Ellis Levy, Beverly Hills, have given $10,000 to form the Rose Lampert Graff Foundation at Cedars of Lebanon Hospital, Los Angeles, for the study of respiratory diseases during 1939. Dr. Jacob J. Singer, Los Angeles, is director of the foundation, which is a memorial to Mrs. Levy's mother. The foundation was organized as a corporation Dec. 14, 1938, and plans are now being considered by the donors to continue it for five years.

Society News.—At a meeting of the Alameda County Medical Association in Oakland June 19 the speakers, all members of the staff of Merritt Hospital, included Drs. William H. Sargent on "Treatment of Skin Cancer with Unfiltered X-Ray"; Frederick E. Blume, "An Unusual Abdominal Tumor"; Lloyd E. Kindall, "Surgical Removal of Renal Calculi," and John N. Ewer, "Trichomonas and Yeast Vaginitis."

DISTRICT OF COLUMBIA

Administrator for Society's Health Service.—Mr. Hugh G. Buhrman, formerly connected with the American Red Cross, has been appointed administrator for the Mutual Health Service of the Medical Society of the District of Columbia. He will occupy quarters in the society's building. Officers of the service are Drs. Archibald L. Riddick, president; Thomas E. Mattingly, vice president, and Mr. Theodore Wiprud, secretary. The service is under the direction of the board of trustees, consisting of Drs. Henry R. Schreiber, chairman; Harry F. Dowling, Augustus Clagett Gray, William P. Herbst Jr., Kate B. B. Karpeles, Luther H. Reichelderfer and Drs. Riddick and Mattingly.

FLORIDA

Society News. — The Dade County Medical Society was addressed at a recent meeting by Drs. Arthur H. Weiland, Coral Gables, on "Internal Fixation of Transcervical Fractures of the Hip" and Lynn W. Whelchel, Miami, "Treatment of Severe Acidosis in Children."——At a meeting of the DeSoto-Hardee-Highlands County Medical Society recently in Wauchula, Dr. Julian L. Hargrove, Bartow, spoke on "Operation for Rupture of Gastric Ulcers."——The Duval County Medical Society was addressed recently by Drs. Turner Z. Cason and Robert H. Cox Jr., Jacksonville, on "Diabetes Mellitus: Analysis of Cases Treated in the Outpatient Department of the Duval County Hospital During the Past Twelve Years."——At a recent meeting of the Leon-Gadsden-Liberty-Wakulla-Jefferson County Medical Society recently in Wakulla Springs, the speakers were Drs. Harold P. McDonald, Atlanta, on "Prostatic Obstruction and Its Treatment"; Albert O. Linch, Atlanta, "Treatment of Ingrowing Toe Nails"; Francis T. Holland, Tallahassee, "Report of Three Cases of Rheumatic Fever," and Edward R. Annis, Tallahassee, "Hypertensions in General Practice."——A recent meeting of the Pinellas County Medical Society was addressed by Dr. Louis B. Mount, St. Petersburg, on "Granuloma Inguinale." Dr. Daniel M. Hoyt, St. Petersburg, addressed the society recently on "Endemic Typhus."——Dr. Exum B. Walker, Atlanta, discussed "Practical Aspects of Common Neurosurgical Problems" before the Polk County Medical Society recently in Lakeland.

GEORGIA

Society News.—Dr. John D. Bradley discussed "Bronchial Asthma with Special Reference to Some of the Newer Drugs" before the Macon Medical Society of Bibb County, Macon, May 16.——At a meeting of the Georgia Medical Society, Savannah, May 9, Dr. Ruskin King read a paper entitled "Abdominal Pain in Children" and Dr. Sherwood C. Lynn reported a case of "Complications of Pneumothorax."—— Dr. Columbus H. Barnwell, Chattanooga, Tenn., addressed the Walker-Catoosa-Dade Counties Medical Society May 1 in Ringgold on "The Latest Treatment for Urinary Disease." Dr. David Lloyd Wood, Dalton, also spoke.

Health Program Expanded.—Public health services will be available to all the counties of the state in accordance with a new plan in which the U. S. Public Health Service, U. S. Children's Bureau, the counties of the state and the Georgia Department of Public Health are cooperating. Effective July 1, funds will be provided to the counties through a graduated health budget, allotted proportionately as the size of the county indicates its need for financial aid. The state will be divided into six districts, each to be in charge of a district health unit composed of a medical director, sanitarian, public health nurse and clerk. All health activities in the unorganized counties of under 14,000 population not employing a full time health commissioner will be supervised by the new district unit.

ILLINOIS

Personal.—Dr. Harrison C. Blankmeyer has been appointed superintendent of health of Springfield.—— The Community Club of Hampshire sponsored a farewell party June 8 in honor of Dr. and Mrs. Frank A. Olms, who were leaving for Florida. Mrs. Olms was presented with a handbag and Dr. Olms with a watch on which was engraved "From Hampshire Community to Dr. Olms, 1907 to 1939." A check was also presented to the couple.——Dr. John P. Roark, Bushnell, was honored at a combined meeting of the Fulton and McDonough county medical societies recently. Dr. Harold M. Camp, Monmouth, secretary, Illinois State Medical Society, presented Dr. Roark with a medal and a certificate of membership in the fifty year club of the state society.

Chicago

Annual Golf Tournament.—The Chicago Medical Society will hold its annual golf tournament at Olympia Fields Country Club August 2. The many prizes include the Chicago Medical Society Championship Trophy for the lowest gross score; the VanDerslice Trophy, to be awarded to the officer or councilor with the lowest gross score; the Sisson Trophy to be awarded to and to become the permanent possession of the doctor, whether member or officer, with the lowest net score, and the Hospital Championship Trophy, to be awarded to the hospital with the winning hospital foursome. This last prize is being awarded this year for the first time.

Dr. Bailey Goes to University of Illinois.—Dr. Percival Bailey, professor of surgery and neurology, Department of Medicine, Division of Biological Sciences, University of Chicago, has been appointed professor of neurology and neurologic surgery at the University of Illinois College of Medicine. Dr. Hans Brunner, formerly chief of the ear, nose and throat department at the Policlinic of Vienna, has been appointed assistant professor of otolaryngology on a half time basis. Both appointments are effective September 1. These newly created positions are a part of the medical school's expanded program in neuropsychiatry under the direction of Dr. Eric Oldberg, now under way with the construction of a neuropsychiatric institute on the grounds of the Research and Educational Hospital (THE JOURNAL, Aug. 27, 1938, p. 851). Dr. Bailey graduated at Northwestern University Medical School in 1918. He has been professor at the University of Chicago since 1933. Dr. Brunner graduated at the University of Vienna in 1919, later serving on the staffs of the University Clinic of Surgery, Vienna, and the Policlinic of Vienna. During the year 1938-1939 he has been an intern in the Research and Educational Hospital.

MAINE

Personal.—Dr. Ralph S. Belmont, formerly associate medical officer, U. S. Veterans' Administration, West Los Angeles, Calif., has been appointed health officer of the town of Sanford, it is reported.

Society News.—At a meeting of the Washington County Medical Society in Eastport May 25 Dr. Harrison L. Robinson, Bangor, discussed "Epigastric Surgery" and Harold Pressey, Bangor, physical therapy.—— The Piscataquis County Medical Society was addressed in Guilford May 25 by Dr. Allan Woodcock, Bangor, on "Fractures of the Femur."—— The Portland Medical Club was addressed recently by Dr. Benjamin Zolov on "Sulfapyridine and Sulfanilamide in the Treatment of Pneumonia."

MICHIGAN

Odd Fellows Offer Service as Blood Donors.—Members of the Independent Order of Odd Fellows throughout Michigan are offering their services as volunteer blood donors without charge. The order hopes with the cooperation of the various medical societies in the state to maintain a central list of volunteer donors in each county. According to the *Bulletin* of the Genesee County Medical Society, it is the wish of the order to make its services available whenever required for indigent persons. In the instances in which persons can pay for the service, the money will be used for charitable purposes.

Traffic Safety Training.—The second national institute for traffic safety training will be held at the University of Michigan, Ann Arbor, August 14-26. Sponsoring organizations include the American Automobile Association, American Association of Motor Vehicle Administrators, American Association of State Highway Officials, American Public Works Association, Automotive Safety Foundation, Highway Education Board, Institute of Traffic Engineers, International Association of Chiefs of Police, National Safety Council, Northwestern University Traffic Institute and Yale University Bureau for Street Traffic Research. Further information may be obtained from Sidney J. Williams, 20 North Wacker Drive, Chicago.

Postgraduate Instruction.—Two periods of postgraduate training for practitioners will be available at Receiving Hospital, Detroit, September 17-November 11 and November 12-February 3, under the auspices of the Wayne County Medical Society, Wayne University College of Medicine and the staff of the hospital, according to an announcement from the society. Physicians will meet once a week for ward rounds stressing bedside diagnosis and treatment of medical cases. The course aims to give the practitioners in groups of not more than six opportunity to examine and discuss a wide variety of clinical material at the bedside. Dr. Gordon B. Myers, professor of medicine at the university, will direct the program with members of the staffs of the medical school and the hospital participating. There will be no fee.

MINNESOTA

Gold Medal Awarded to Dr. Hart.—The Southern Minnesota Medical Association presented its annual gold medal to Dr. Vernon L. Hart, Minneapolis, for the best scientific exhibit at the Minnesota State Medical Association. Dr. Hart's subject was "Fracture Problems." Dr. Hart is a graduate of the University of Michigan Medical School, Ann Arbor, where he served from 1929 to 1932 as assistant professor of surgery. He has been an instructor at the University of Minnesota Medical School since 1933.

MISSOURI

Physicians Appointed to Boards.—Recent appointments to the state board of health include those of Drs. Charles H. Neilson, St. Louis; Edward Sanborn Smith, Kirksville; George W. Gay, Ironton; John Aull, Kansas City, and William M. West, Monett. Dr. Doyle C. McCraw, Bolivar, has been appointed a member of the board of managers of eleemosynary institutions; Dr. Charles E. Hyndman, St. Louis, a member of the board of nurses' examiners, and Drs. Frederick J. Taussig, St. Louis, and Paul F. Cole, Springfield, members of the state cancer commission.

Society News.—The Six County Medical Society was addressed June 15 in Sikeston by Drs. Carliss M. Stroud on hay fever and Garold V. Stryker, common skin diseases; both speakers are from St. Louis. This society is composed of Dunklin, Butler, Pemiscot, Mississippi, New Madrid and Scott counties, meeting once each year in a different county. There is only one officer of the six county organization, that of secretary, which this year is held by Dr. Lawrence E. Cooper, Cooter. At each meeting of the society the president of the county society which acts as host serves as president and chairman of the assembly.

NEBRASKA

District Meetings.—The Tenth Councilor District Medical Society met in Hastings recently with the following speakers: Drs. Louis R. Nash, Ingleside, on new therapy in pneumonia; Albert F. Tyler, Omaha, high voltage x-ray therapy; Horace W. Shreck, Holdrege, infections of the bladder, and John H. Waterman, Ingleside, play therapy.——Drs. Esley J. Kirk and Joseph A. Weinberg, Omaha, addressed the Sixth Councilor District Medical Society in York recently on "Diagnosis and Management of Nephritis" and "Radical Surgery of the Breast" respectively.

NEW JERSEY

Personal.—Dr. Joseph S. Van Dyke, Palisades Park, was honored at a dinner at the Knickerbocker Country Club June 22 in celebration of his twenty-five years of service as chief of the women's medical service and twenty-nine years on the staff at the Englewood Hospital. The dinner was given by the hospital staff.

Society News.—Dr. Pauline A. Long, New Brunswick, was reelected president of the New Jersey Medical Women's Association at the annual meeting in May. Drs. Grace W. A. Holmes, Elizabeth, and Eva T. Brodkin, Newark, were elected vice presidents and Dr. Elizabeth B. Ward, Newark, was made secretary.

NEW YORK

Personal.—Dr. Arthur J. Bedell, Albany, recently delivered an address before the Ophthalmological Society of the United Kingdom in London on "Fundus Changes in Diabetes."——Drs. Duane E. Ensign, McGraw, and John E. Leonard, Harford Mills, were honored by the Cortland County Medical Society at a dinner June 16 at the Cortland Country Club celebrating their completion of fifty years of medical practice. Dr. Ensign began practice in the county in 1888 after graduation from Eclectic Medical Institute, Cincinnati, and Dr. Leonard in 1889 after his graduation from the Long Island Medical College. Dr. Bert R. Parsons, Cortland, was toastmaster at the dinner.——Dr. Gustave A. Fensterer, Garden City, was honored by the Medical Society of the County of Nassau recently by the presentation of a plaque honoring him as a founder and the first president of the society.——Dr. Charles Rich, Yorktown Heights, was honored by friends and patients recently on his completion of fifty years of practice by the presentation of a silver tray.

New York City

County Society Makes X-Ray Study at World's Fair.—The Medical Society of the County of Queens is making x-ray studies of visitors to the World's Fair, using paper films. The films are read by a committee of radiologists and the report is forwarded to the subject's own physician. Any one who cares to register may have the roentgenogram made. The chairman of the society's committee in charge of this project reported May 23 that up to that date 320 plates had been read and in sixty-seven of them abnormalities needing medical attention were found.

Degree in Forensic Medicine.—Dr. Maurice Powers, Regina, Sask., Canada, received the first degree of doctor of medical science in forensic medicine to be awarded by New York University College of Medicine June 7. Dr. Powers graduated from McGill University Faculty of Medicine, Montreal, in 1934 and has been director of the laboratory of the Royal Canadian Mounted Police in Regina since August 1937. He was on leave to complete his course in scientific crime detection and medical aid to crime solution. The department of forensic medicine at New York University was reorganized in 1936 to provide graduate instruction leading to the degree of doctor of medical science.

NORTH CAROLINA

Personal.—Mr. Frank W. Webster, Southern Pines, has been appointed managing director of the North Carolina Tuberculosis Association. He succeeds Dr. Romulus L. Carlton, Winston-Salem, who has been acting managing director since August 1937, when the late Dr. Louis B. McBrayer resigned because of ill health. Mr. Webster, a graduate of the University of North Carolina, has been superintendent of schools in Southern Pines. He will maintain the offices of the association in Winston-Salem.——Dr. Herman F. Easom, Raleigh, has resigned as director of the division of industrial hygiene of the state board of health after three and a half years in the position. He will return to the staff of the North Carolina Sanatorium for the Treatment of Tuberculosis, where he was formerly located.——Dr. Carl V. Reynolds, Raleigh, has been reappointed state health officer for another four year term. He was first appointed acting health officer in November 1934 on the death of Dr. James M. Parrott and received the regular appointment in May 1935.——Dr. Charles W. Armstrong, Salisbury, was honored at a testimonial dinner May 16 marking his twentieth anniversary as health officer of Rowan County.

OHIO

University News.—The John and Mary R. Markle Foundation, New York, has made a grant of $4,100 to Western Reserve University School of Medicine to be used by Dr. Carl J. Wiggers, professor of physiology, to study the nature of ventricular fibrillation and means of sensitizing and desensitizing the heart.

Professor Retires.—Dr. John J. Thomas, associate clinical professor of obstetrics, Western Reserve University School of Medicine, Cleveland, retired at the end of the school year June 14, it is reported. Dr. Thomas graduated from Western Reserve in 1893 and has been a member of the faculty for forty-three years. He will continue in private practice and on the staff of St. Ann's Hospital.

Bureau of Public Education Established.—By action of the house of delegates at the annual meeting of the Ohio State Medical Association in May, a bureau of public education has been established in the executive offices of the association in Columbus. Mr. Richard A. Aszling, a graduate of Oberlin College and recently a member of the staff of the Dayton *Daily News*, has been chosen as director of the bureau.

Society News.—Dr. Charles G. Johnston, Detroit, addressed the Wood County Medical Society, Bowling Green, June 15, on "Long Tube Drainage in the Treatment of Intestinal Obstruction."——Dayton physicians addressed the Hempstead Academy of Medicine of Scioto County in Portsmouth June 5 as follows: Drs. Robert C. Austin on "The Breast"; Edgar L. Braunlin, "Radical Removal of the Breast," and Roy S. Binkley, "Solution of the Indigent Relief Situation in Dayton by the Montgomery County Medical Society."——Dr. Hubert C. King, Lakewood, addressed the Lorain County Medical Society, Elyria, June 13 on "Diagnostic Problems in Coronary Heart Disease and Coronary Occlusion."

PENNSYLVANIA

Hospital News.—Gov. Arthur H. James broke ground recently for two new buildings at Eagleville Sanatorium for Consumptives, Eagleville. The sanatorium is supported by state appropriations, funds raised by public subscription and by private funds. The new buildings will replace four obsolete structures built when the institution was founded thirty years ago.

Meeting of Negro Physicians.—The Pennsylvania State Medical, Dental and Pharmaceutical Association, organized in 1921 by Negro practitioners, met in Harrisburg June 30. The program was devoted to cancer, syphilis and tuberculosis, with the following speakers, among others: Drs. John J. Shaw, state secretary of health; Charles S. Everhart, Harrisburg, chief of the division of syphilis in the state department of health; Stanley P. Reimann, Philadelphia; Henry M. Minton, Philadelphia, and Charles Howard Marcy, Pittsburgh.

Philadelphia

Professor Appointed.—Dr. Howard Canning Taylor Jr., associate professor of obstetrics and gynecology at New York University College of Medicine since 1935, has been appointed William Goodell professor of gynecology at the University of Pennsylvania School of Medicine. Dr. Taylor succeeds the late Dr. Floyd E. Keene. He graduated from Yale University, New Haven, and from Columbia University College of Physicians and Surgeons, New York, in 1924. Recently he has been attending gynecologist at Roosevelt Hospital, associate visiting obstetrician and gynecologist at Bellevue and associate surgeon at Memorial Hospital for the Treatment of Cancer and Allied Diseases. A new building for the department of gynecology and obstetrics is under construction at the university (THE JOURNAL, July 23, 1938, p. 330).

Pittsburgh

Society News.—Dr. Louis E. Phaneuf, Boston, addressed the Pittsburgh Obstetrical and Gynecological Society May 20 on "Management and Results of Operation for Prolapse of the Uterus."

Personal.—Dr. Richard J. Behan was honored with a testimonial dinner by the sisters and staff of St. Joseph's Hospital, Pittsburgh, May 15, in recognition of his twenty-five years of service to the hospital.

VIRGINIA

Dr. Landis Appointed Professor.—Dr. Eugene M. Landis, assistant professor of medicine at the University of Pennsylvania School of Medicine, Philadelphia, has been appointed professor of internal medicine at the University of Virginia Medical Department to succeed the late Dr. James C. Flippin. Dr. Landis took his medical degree at the University of Pennsylvania in 1926 and the degree of doctor of philosophy the following year. He held a Guggenheim Foundation fellowship following his internship and has been a member of the Pennsylvania medical faculty since 1931. He has conducted research in the physiology of the circulation, pathogenesis of edema, peripheral vascular disease and renal disease. In 1936 he received the John Phillips Memorial Medal of the American College of Physicians.

Society News.—Dr. Roy D. McClure, Detroit, addressed the Richmond Academy of Medicine May 9 on "Anoxia and What It Means to the Surgical Patient."——Dr. Robert V. Funsten, Charlottesville, addressed the Lynchburg Academy of Medicine recently on "Low Back Pain."——At the annual meeting of the Virginia Pediatric Society in Charlottesville in May speakers included Dr. DuPont Guerry III, New York, on "Effect of Vitamin K Concentrate on Prothrombin Time and Clotting Time in the Newly-Born."——Dr. Henry B. Mulholland, Charlottesville, addressed the Rockbridge County Medical Society, Lexington, May 22 on "Acidosis, Alkalosis and Dehydration."

WISCONSIN

Society News.—Dr. Walter P. Blount, Milwaukee, addressed the Ashland-Bayfield-Iron County Medical Society, Ashland, June 10 on "Prevention of Deformity in Children."——Dr. Charles R. Marquardt, Milwaukee, addressed the Columbia-Marquette-Adams County Medical Society, Columbus, June 20 on "Diseases of the Urogenital Tract."——At a meeting of the Green Lake-Waushara County Medical Society in Berlin June 14 the speaker was Dr. John W. Harris, Madison, on obstetric problems.——Drs. John A. Toomey, Cleveland, and David S. Hillis, Chicago, addressed the Medical Society of Milwaukee County recently on "Treatment of Contagious Diseases Featuring Convalescent Serum" and "Routine Circumcision of the Newborn Infant" respectively.——Dr. Max Cutler, Chicago, addressed the Milwaukee Society of Clinical Surgery recently on "Indications, Limitations and Results of Radiation in the Treatment of Cancer" and Dr. Chester C. Schneider, Milwaukee, on "Osteomyelitis."

GENERAL

Editor of Anatomy Journal Appointed.—Dr. George W. Corner, professor of anatomy, University of Rochester School of Medicine and Dentistry, Rochester, N. Y., has been appointed managing editor of the *American Journal of Anatomy* to succeed the late Dr. Charles R. Stockard, New York.

Dietetic Meeting.—At the annual meeting of the American Dietetic Association in Los Angeles August 28-31 the speakers will include: Drs. Albert H. Rowe, Oakland, on "Use of the Elimination Diets in the Diagnosis and Treatment of Food Allergy"; William D. Sansum, Santa Barbara, "The Treatment of Diabetes Mellitus," and Herbert M. Evans, Berkeley, "Vitamin E in Human Nutrition."

Symposium on Growth.—The editors of the journal *Growth* announce a symposium on growth and development to be held at North Truro, Mass., August 7-11. Subjects to be discussed are: cell division and differentiation, genes and development, chemical factors, regeneration and organization, and concept of the organism. Among the speakers listed are: Dr. Warren H. Lewis, Baltimore; Paul W. Gregory, Sc.D., Davis, Calif.; Curt Stern, Ph.D., Rochester, N. Y., and Edmund W. Sinnott, Ph.D., New York.

Industrial Hygiene Society.—At the third annual American Conference on Occupational Diseases and Industrial Hygiene, held in conjunction with the meeting of the American Association of Industrial Physicians and Surgeons in Cleveland in June, a permanent organization was formed, the American Industrial Hygiene Association. William P. Yant, research director of the Mine Safety Appliances Company, Pittsburgh, was elected president; Warren A. Cook, Zurich General Accident and Liability Insurance Company, Chicago, president-elect, and Gordon C. Harrold, Ph.D., Detroit, Industrial Hygiene Laboratories, Chrysler Corporation, secretary.

Changes in Status of Licensure.—The California State Board of Medical Examiners announces the following actions taken at its meeting in February:

Dr. Milton F. Novotny, Burlingame, placed on probation for five years with the understanding that he cease practice immediately and not resume practice until Aug. 1, 1939; that he not be permitted to apply for or have a federal narcotic permit or have narcotics in his possession.

Dr. Harvey Smith, Los Angeles, placed on probation for five years with the understanding that he abstain from all alcoholic beverages, for conviction of driving while intoxicated.

Dr. Joseph T. Wrenn, San Francisco, license revoked, provided that if he immediately file a stipulation with the board that he would not aid or abet an unlicensed individual, nor advertise other than by the use of the ordinary business card, said revocation would be set aside and he would be placed on probation for a period of five years; he was charged with aiding and abetting an unlicensed practitioner, namely William Van Buren.

Dr. William H. Young, San Francisco, license revoked on two charges, aiding and abetting and use of a fictitious name in connection with the so-called Samaritan Treatment for Alcoholism, San Francisco branch.

Award for Chemical Research.—Dr. Nathan B. Eddy, research professor of pharmacology, University of Michigan Medical School, Ann Arbor, and Lyndon F. Small, Ph.D., research associate in organic chemistry, University of Virginia, Charlottesville, received the 1938 award of the American Pharmaceutical Manufacturers Association at the annual meeting at Skytop, Pa. This award, presented for the year's most outstanding chemical research, went to Dr. Eddy and Dr. Small in recognition of their work on substitutes for morphine. The research has been conducted under the auspices of the U. S. Public Health Service as part of a study of habit-forming narcotics directed by the committee on narcotic addiction of the National Research Council. The investigations at Michigan and Virginia have been aided by funds from the Rockefeller Foundation. U. S. Commissioner of Narcotics H. J. Anslinger made the presentation of the award.

Special Society Elections.—Dr. David E. Robertson, Toronto, Ont., was named president-elect of the American Orthopedic Association at the annual meeting in Buffalo June 5-8 and Dr. Frank D. Dickson, Kansas City, became president. Dr. Wallace H. Cole, St. Paul, was elected vice president and Dr. Ralph K. Ghormley, Rochester, Minn., was reelected secretary.——Dr. Foster Kennedy, New York, was elected president of the American Neurological Association at the annual meeting in Atlantic City and Drs. Stanley Cobb, Boston, and Henry W. F. Woltman, Rochester, Minn., were elected vice presidents. Drs. Henry Alsop Riley, New York, and Bernard J. Alpers, Philadelphia, were reelected secretary and assistant secretary, respectively.——Dr. Douglas A. Thom, Boston, was elected president of the American Psychopathological Association at the annual meeting in Atlantic City June 6; Drs. George S. Sprague, White Plains, N. Y., and Bernard Glueck, New York, were elected vice presidents and L. Eugene Emerson, Ph.D., Boston, was reelected secretary.

Award of Anna Fuller Prize.—Trustees of the Anna Fuller Fund have announced the first award of the Anna Fuller Memorial Prize of $7,500 to a group of five scientists at the Research Institute of the Royal Cancer Hospital of London: Dr. Ernest L. Kennaway, director of the institute; James Wilfrid Cook, Colin Leslie Hewett and Izrael Hieger, chemists, and William Valentine Mayneord, physicist. This fund was established in 1931 in the will of Egbert C. Fuller of Branford, Conn., who left a trust fund of $1,500,000 for alleviation of suffering from disease and especially for the control of cancer, in memory of his wife, who died of cancer in 1918. Mr. Fuller instructed that the prize should be given "to such person or persons as shall at any time, within successive periods of five years each, commencing one year after my death, make a real and outstanding contribution to knowledge on the subject of cause, care, prevention or cure of cancer." The award was made on the recommendation of the President of the American Medical Association, the dean of Johns Hopkins University School of Medicine and the dean of Harvard Medical School. The committee this year was made up of Drs. Irvin Abell, Louisville, Ky., Alan M. Chesney, Baltimore, and Charles Sidney Burwell, Boston.

Foreign Letters

LONDON

(From Our Regular Correspondent)

July 5, 1939.

The Timing of Symptoms

In a lecture to the Medical and Physical Society of St. Thomas's Hospital on "The Timing of Symptoms," Prof. J. A. Ryle said that the subjective phenomena of disease have a value for the physician which, in the course of time, comes to exceed by far the value of objective signs, and that they proclaim physiologic disturbance which may or may not be due to organic disease. Effort pain in the chest (angina pectoris) is now believed to be the expression of oxygen want in the heart muscle. "Symptoms are universally available; they are the voice of nature," said Dr. John Brown. But they present two difficulties: they cannot be measured and they cannot be studied in animals. But one of their attributes—their timing—lends itself to measurement and has high diagnostic value. Professor Ryle discussed the timing of four classic types of pain: angina pectoris, hunger pain, renal colic and intestinal colic.

ANGINA PECTORIS

The angina of effort lasts as a rule from two to five minutes, but the status anginosus of coronary occlusion may last for hours or return in repeated storms for a day or two. In the former the conclusion has been reached, on the basis of Lewis's teaching, that narrowed or inelastic vessels fail to transmit sufficient oxygenated blood on effort. The cessation of effort restores the balance. But in coronary thrombosis the pain continues until local death of the muscle occurs and the collateral circulation brings relief. A pain of intermediate duration is encountered in patients who have had angina pectoris for a long time. Here one is entitled to visualize increased narrowing or rigidity of vessels so that the balance is less quickly restored. Eventually angina may trouble the patient at rest, particularly in the early morning. Is this due to shallow breathing during sleep or to emotion operating through dreams?

HUNGER PAIN

The hunger pain of duodenal ulcer is held to depend on exaggeration of peristalsis of the pyloric antrum when the stomach is empty or approaching emptiness. But it may also be due to other irritative lesions, such as cholecystitis, or more rarely in early pyloric carcinoma and in nervous states. If no food or medicine is taken it may last for an hour or more and when relieved by food the interval to the next pain is usually between two and three hours but in the case of rapidly emptying stomachs may be as short as an hour. The frequency and periodicity of the pain depend on the food habits of the individual. When pyloric stenosis develops the time interval alters; the pain occurs soon after food from the effort of the stomach to overcome the obstruction.

RENAL COLIC

The factors which determine the arrival of a stone at the pelviureteral junction or in the ureter must be numerous. Attacks therefore come "out of the blue" at no special time, except that they are prone to be nocturnal like Heberden's other "spasmodic complaints." The pain is sustained and crescendo, rarely intermittent. The term colic is therefore misleading. On the other hand, intestinal colic recurs rhythmically in spasm—in obstructive cases at intervals of three or four minutes and lasting a few seconds.

The Cancer Problem

Speaking on behalf of the Empire Day Appeal of the British Empire Cancer Campaign, Dr. Walter Elliot, minister of health, said that the rise in the number of deaths from cancer, progressive for many years and reaching 74,000 in 1937, could not be disregarded. Though this increase could be explained largely but not wholly by the growing average length of life, for cancer attacked the middle aged and the old more than the young, that was small comfort. A concerted attack on the disease was clearly necessary and took the form of the Cancer Act. Many patients did not receive appropriate treatment or did not receive it until cure became impossible. For this there were many reasons. There was a deficiency of centers with facilities for modern treatment. The Cancer Act would remove or lessen many of these difficulties. The new cancer service, which extended facilities for treatment, would provide greater opportunities for clinical research.

Mr. Cecil Rowntree, surgeon to the Cancer Hospital and vice chairman of the campaign, said that there was evidence of progress all along the line. For some months he had been helping to arrange for an International Cancer Congress at New York. He had received a letter from the president of the New York committee, who said "The German delegates are definitely coming to the conference and their subscriptions have been forwarded."

Committee of Research in Preventive Medicine

The Medical Research Council has appointed a committee to advise and assist it in promoting research into problems of preventive medicine. The members include specialists in various branches—clinical medicine, immunology, nutrition and vital statistics—and health officers from different parts of the country, including members of the medical staff of the Ministry of Health. The chairman is Sir W. Wilson Jameson, dean of the London School of Hygiene and Tropical Medicine. Among the members are E. H. Harries, chief medical superintendent, Infectious Hospitals Service, London; A. Bradford Hill, university reader in epidemiology and vital statistics, London School of Hygiene and Tropical Medicine; R. M. F. Picken, professor of preventive medicine, Cardiff, and W. W. C. Topley, professor of bacteriology and immunology, London School of Tropical Medicine and Hygiene. Three years will be the normal period of service on the committee.

BERLIN

(From Our Regular Correspondent)

May 15, 1939.

The New Leader of German Physicians

As previously reported, Dr. Wagner, leader of the physicians of the reich, recently died. Dr. Leonardo Conti has been appointed as his successor with the title "health leader of the reich." Dr. Conti was born in 1900 in Lugano (Italian section of Switzerland) and bears an Italian first name and family name. His mother was well known in Berlin as a midwife and now plays a leading part in directing the midwives. Dr. Conti was co-founder and secretary of the first anti-Semitic club organized in Berlin in postwar days. In 1923 he became an S A follower. In 1927 he joined national socialism and became the first S A physician in Berlin. Later on he was leader of the Berlin district of the national socialist medical association. In the upheaval of 1933 he was assigned to the ministry of the interior. He engaged in lecturing, for example, on the prohibition of vivisection (he was in favor of rendering scientific experimentations on animals more difficult), on the position of the physician in the third reich and so on. Since 1936 he has been in charge of the health department of the city of Berlin. He now takes Dr. Wagner's place. The change of title is to indicate the change in the status of the physician in the new régime. The most important task assigned to the physician by the political party in control is not to cure illnesses and diseases but to "serve by promoting health and preventing disease."

Nonspecific Encephalitis

Prof. Ulrich Fleck recently pointed out, at a meeting of the medical society of Nuremberg, the difficult clinical situation as regards nonspecific inflammations of the brain. Fleck was for many years assistant in the psychiatric clinic of Göttingen and has gathered valuable information in this field, as this clinic gave special attention to these problems and for many years possessed a special division of encephalitis research. Altogether, Fleck was able to observe fourteen patients in the last three years in the psychiatric and nerve clinic of Nuremberg, which he now directs. These patients included not only youthful ones but some as old as 45 years. The symptoms which Professor Fleck reports are in part quite insignificant. They are limited in certain cases to an indication of pyramid formations, but cerebellar and clearly spastic manifestations may set in. Six of the patients showed leukocytosis, five nystagmus, two double images and four very clear changes in the fundus oculi in the sense of a choked disk. The temperature did not indicate any essential heightening. Puncture yielded in part a considerable increase in the cell count, in some cases also a strong increase of albumin content, and showed mastic curves like those of syphilis. Two of the patients died. One showed perivascular infiltrations which in their distribution came close to conforming to Spatz's type of epidemic encephalitis. In the second patient there were found only clear meningeal infiltrations. The other patients improved more or less after a few weeks and in even a shorter time. According to the anatomic observations these disorders cannot be identified with those of the type of encephalitis japonica (THE JOURNAL, Sept. 10, 1938, p. 1030). In contrast with the latter the cerebrum and cerebellum were not affected; the white substance was likewise completely free of infiltrations.

Heredity and Race

Discussion on heredity and race has become relatively quiet since the pertinent laws and regulations have been passed and executed with the well known thoroughness. A few new facts are to be reported because they throw a strong light on conditions here:

First, in an essay composed by the director of "Practical Race Politics" in the department of Race and Politics of the national socialist party, he discusses the term "hereditarily undesirable." He states that finally the demands long insisted on by his department have been incorporated into the legislation of the reich. According to these, not only the hereditary condition of health or disease of the individual but also his kin determines the hereditary worthwhileness of the individual. In other words, it includes what is comprehended under the term "hereditarily fit." The governmental department of Race and Politics has always insisted, he went on to say, in the last years that an industrious, decent and capable family of many children should not be regarded as hereditarily unfit because one of the children perhaps suffered from a physical defect or a feebleminded child was found among well gifted children. On the other hand, it has become clearer in the last years that the terms "hereditarily healthy" and "hereditarily diseased" in the narrow medical sense are by no means identical with the terms "hereditarily desirable" and "hereditarily undesirable." At the utmost from 20 to 25 per cent of the members of asocial large families that threaten the stability of the German people are hereditarily diseased in the meaning of the law. It is precisely the "hereditarily healthy" members of asocial large families that radically menace the German nation. Not only do nearly all growing children in typically asocial large families show defects, but proof can be furnished that heredity is involved. These observations have been confirmed during the last years through experiences in the selection for the "Honor Book for Large Families."

Recent decisions of two higher courts relative to the famous paragraph 218 of the penal laws should prove of interest. This paragraph deals with abortion and is now strictly enforced. These courts expressly stated that paragraph 218 continues to apply to Jewish women, since the "sure order of political life demands it, although the state, because of its present principles governing the growth of population, has no interest in the birth of Jewish children and would even regard it as desirable if the expected child did not see the light of day. However, the free and unregulated permission of abortion cannot be granted persons of Jewish extraction living in Germany, however undesirable the birth of Jewish children might be." All principles of a medical and social nature which require combating abortion, therefore, do not apply in this case, but only party politics.

These discussions, though apparently purely of a legal nature, concern the physician after all, since they rest on a pretended biologic conception of the racial idea. For this reason, in conclusion, a report is made of the joint session of German and Italian lawyers which took place in March of this year in Vienna in pursuance of the "German-Italian cultural pact" and was attended by the leading jurists of both nations. So much importance was attached to this session that reports appeared also in German medical periodicals. The following fundamental principles were authoritatively laid down at this session: National socialism does not proceed by defending the race through the law but by securing and strengthening the blood order of the German people. To accomplish this the following measures are necessary: (1) to bind law to the race idea and to create a jurisprudence based on racial laws; (2) in the establishment and application of law the cultivation of heredity and race must be placed in the center of all measures.

Eye Injuries

Dr. Brüning reported statistically on the cases of eye injuries treated in the last fifteen years at the Klinik für Augenkranke of the University of Berlin. The following conclusions were drawn: The number of patients tends to correspond to economic conditions. The number of those injured during working hours has increased in the last years. Injuries distinctly increase in summer and around the middle of each week. Hourly distribution reveals an increase during the busiest working hours, with slight emphasis on the morning hours. Grouped according to age, the second decade predominates. Eye glasses are not dangerous for the worker or the motorist; not one case of eye injury to a motorist by splinters from his own glasses has been found in fifteen years. This fact is important because the authorities are considering permitting motorists to wear glasses made of safety glass only.

Consultations for Pregnant Women

The new law on midwives made the advising of pregnant women a duty of German midwives. The national organization of midwives has now ordered every midwife to advise all pregnant women who request advice, which must be given whether it can be paid for or not. An average of three consultations is regarded as necessary during the period of pregnancy. Certificates of pregnancy for use before the national socialist bureau of national welfare have to be issued without cost.

Institute of Research for Rural Hygiene

In a farm home, the birthplace of Pettenkofer, in Bavaria, an institute of research for rural hygiene will be set up, with efforts directed to improving the living conditions of peasants. The work of this institute is to comprehend thousands of farms and villages in the upper region of the Danube. The topics studied will include questions of habitation and clothing, recreation and diet.

AUSTRALIA

(From Our Regular Correspondent)

June 7, 1939.

Medicosocial Problems in New Zealand

The New Zealand government and the medical profession have not yet reached any agreement over the medical provisions of the social security act. It will be remembered that the prime minister, Mr. Savage, soon after the triumphal return of his party from the polls threatened that if members of the profession would not willingly obey the government they would be forced to do so. Later some modifications of the original plan were promised to meet the opposition of the British Medical Association. But there is still no sign of agreement. This is easily understood when it is considered how utterly opposed are the ideas of the two parties. To the socialistic government it is fundamental that the scheme should provide equal service for everybody. But the universal nature of the plan is its chief objection in the view of the medical profession. Because of the extensive economic repercussions involved and their intimate relation to government policy as a whole, it is impossible to appreciate fully the medical situation in New Zealand without considering the country's economic position generally.

New Zealand, during the past three years, has presented the world with an excellent example of an orthodox system fighting economic planning and unorthodox methods of finance. There is every sign and indication that, up to the present at any rate, orthodoxy is still firmly seated in the saddle. In other words, many of the ideals and aspirations which carried the New Zealand labor party on the crest of the wave into safe anchorage had gradually to be jettisoned in order to keep the ship of state on an even keel.

There are three distinct schools of thought in New Zealand today: 1. Those who are prepared to fight unorthodox methods of finance and political economy to the last ditch and with every means at their disposal; this is the element which suffered overwhelming defeat at the last two general elections. 2. Those who, by steering a middle course of compromise, are endeavoring to implement unorthodox economic measures of reform without unduly interfering with orthodox finance; these comprise a certain section of the labor party headed by the leaders of the government. 3. That other section of the party and its supporters—generally referred to as "left wingers"—who are still adhering to the original pledges of the party and insist that the promises made to the electors should be given effect to. There is good reason for believing that the orthodox element—a minority but influential section of the community—is gaining ground and is benefiting by the adverse conditions, which are not only seriously hampering the government but are lowering its prestige in the eyes of its supporters. Although the government has brought in a number of industrial reforms and social improvements, the policy measures that really counted and that formed the backbone of labor's preelection platform have not yet materialized. At present the government is faced with three serious problems in which the London money lenders, the New Zealand importers and the members of the New Zealand branch of the British Medical Association play an important part.

Even the friends of labor readily admit today that the government's financial difficulties are mainly due to an attempt to implement unorthodox economic and industrial measures without straying from the narrow path of orthodox methods of finance. By means of these reforms the government succeeded in providing employment and raising the standard of living of the masses of the people. At the same time, however, by relying entirely on an unorthodox method of finance and allowing a large volume of capital to be sent out of the country, it found sterling funds overseas rapidly depleted. With loans amounting to £17,000,000 falling due in London in the near future the government made a desperate effort in the eleventh hour to replenish its London funds by restricting and in many instances totally prohibiting imports. It is hardly necessary to elaborate on the effect such a revolutionary policy had on an important section of the commercial community in a country where manufacturing industries are so poorly developed. Next in importance to the government's financial policy comes the social security legislation, so dear to the prime minister's heart. Here again the realization of a highly humanitarian policy bristles with difficulties. By far the most important part of the social security scheme is the new state medical service, and the attitude of the members of the British Medical Association creates a great deal of heart burning in government circles. The state maternity service, which is really the first instalment of the new medical system created by the social security legislation, was introduced early in May, and only forty doctors out of about 900 answered the call. Such a poor response does not at all augur well for the successful launching of the main scheme.

These few instances are sufficient to indicate the difficulties confronting a government that is earnestly seeking to bring about greater economic security and better social conditions for the masses of the people. In matters that really count the government is fighting a losing battle with orthodoxy: a battle with a powerful system which, during the last century, has broken many governments. The men who hold the purse-strings in London are, in a measure, dictating the future policy of New Zealand. The conversion of the £17,000,000 loan and the depleted coffers of the New Zealand Reserve Bank in London will enable them to drive a hard bargain.

Although it was the main plank in the government's preelection program, little is heard of monetary reform in New Zealand today. Even the prime minister's oft repeated references to the utilization of the public credit are things of the past. Driven no doubt by *force majeure*, the labor government promises to become as orthodox as any government New Zealand has ever had. It is true that it was instrumental in raising wages, shortening working hours, increasing pensions and reducing unemployment. But from present indications it would hardly be correct to say that it based these benefits on a sound and lasting foundation. Just as the social security scheme lacks the all important cooperation of the medical profession, so the government's industrial and economic planning lacks the all important cooperation of capital, and in neither case has the government shown sufficient courage or foresight to provide a substitute.

There are many supporters of labor who blame the government for the predicament it finds itself in today: for not taking complete control of the monetary system, for not making use of the public credit, for allowing between £10,000,000 and £15,000,000 of capital to leave the country, for not compelling the medical profession to comply with the state medical service, for prohibiting imports and dislocating the import business, for increasing taxation unduly and raising the cost of living and so on—in short, for not keeping the promises made to the electors and not carrying into effect the mandate given it by the people. But few know of the struggle that is going on behind the scenes; the age old fight between a powerful and influential minority endeavoring to maintain the status quo, thereby refusing to recognize change as an inevitable corollary of progressive development, and a less influential majority, "the masses," who, made aware at first hand of the changing needs of a changing society, must continually strive to keep social development apace with material development.

STOCKHOLM

(From a Special Correspondent)

July 1, 1939.

The Organization of Pneumonia Research

Since the discussion in September 1938 before the Swedish Medical Society on the treatment of pneumonia, attempts have been made to coordinate research in order that comparable data may be available in the different Swedish hospitals. At present the chief difficulty arising over a given case of pneumonia is to decide between the conflicting claims of serum on the one hand and some sulfanilamide preparation on the other. Professor Hilding Berglund, of the St. Erik Hospital in Stockholm, has issued a memorandum on the diagnosis and treatment of acute pneumonia. Without wishing to stereotype the diagnosis and treatment he has realized that, if all the Swedish hospitals were to accept more or less identical procedures, it should be possible to settle the conflicting claims of serotherapy and chemotherapy at a comparatively early date. Preliminary to treatment he recommends the conjunctival test and he requires information concerning the patient's liability to such allergic phenomena as hay fever and urticaria. The contraindications for the administration of horse serum are listed, the indications are mentioned, and advice is given concerning measures to be taken to combat a serious fall of blood pressure. From serum treatment Professor Berglund turns to consideration of chemotherapy. When the pneumococci have been typed and all the other bacteriologic and clinical data have been collected, there may yet be grave doubts as to the treatment to choose. Professor Berglund is opposed to a combination of serotherapy and chemotherapy at present and as long as the relative merits of the two procedures are still in doubt. In early cases in which the type of the infecting organism is definitely established he recommends serotherapy. If that is not available, sulfapyridine should be given, four tablets, each of 0.5 Gm. being given at first, the same dose four hours later, and thereafter two tablets every four hours under close observation, the treatment to be continued for not longer than two days. In fulminating type III pneumonia, very large doses of serum should be preferred to sulfapyridine.

Swedish Wells

The revived interest in the water supplies of country districts reflects to some extent the suspicion that the ravages of infantile paralysis during the last few years are connected with water and water courses. Prince Carl, the enterprising head of the Swedish Red Cross Society, has used his influence in focusing attention on the provision of healthful drinking water in rural areas and has encouraged comprehensive expert surveys of wells and springs in different parts of the country. A survey was carried out in 1938, in the county of Kalmar, by Dr. A. Bergstrand, whose report on 400 wells makes disquieting reading. In more than half of them he found inadequate protection from pollution. In only five instances did he find natural springs the water of which was kept comparatively pure by its free circulation. All the other wells were more or less artificial and as many as five different methods of drawing the water from them were practiced. Everywhere deplorable conditions were detected, and it is to be hoped that country dwellers will be made more well conscious by Dr. Bergstrand's disclosures.

The Late Professor Samuel Hybbinette

Early this year one of the most beloved personalities in the Swedish medical world passed away. Samuel Hybbinette was no ordinary man, and his career was in many respects as unorthodox and unexpected as it could possibly have been. Inconspicuous as a student and hospital intern, he completed his postgraduate training abroad. In 1908 he settled in Stockholm without any important hospital appointment. As his surgical practice grew, word went round among his colleagues about his marvelous dexterity as an operator whose minute knowledge of anatomy was, perhaps, the key to the riddle. He was as surprised as any one when he learned in 1921 that he had been chosen to succeed Prof. Gunnar Nyström as chief of one of the surgical services of the Sabbatsberg Hospital in Stockholm. Skepticism as to the truth of printed words, even when found in standard textbooks, may have had an inhibitory influence on his writings, the quantity of which was inversely proportional to their quality. He made important contributions to the treatment of fractures and he devised an operation for recurrent dislocation of the shoulder joint, now known as the Eden-Hybbinette operation. He did much to perfect operations for cleft palate and harelip. His own palate was as delicate and fastidiously discriminating as were his fingers (he came of French Huguenot stock) and he was known to a wide circle of friends as a gourmet, combining science and art most happily in this domain. His voice was wonderful, and he took every opportunity to keep it trained. Hardly a day passed in his busy life without his giving infinite pleasure to those who heard him sing. February 12 he was celebrating in his club the successful debut of his son, a law student, as a singer. The party was coming to an end just after midnight, and Hybbinette was joining with others in a choral tribute to the shades of the departed when he collapsed and died.

Marriages

CHARLES H. STUBENRAUCH JR., Havana, Ill., to Miss Louise Stiegemeyer of Champaign at Tuscola, June 26.

RAYMOND TAYLOR JENKINS, Fort Bragg, N. C., to Miss Blanche Brickle of Black Mountain, June 10.

FRANCIS ALVA ELLIS to Miss Margaret Cecelia Bautz, both of Baltimore, at Washington, D. C., July 1.

CARL ALDEN SWEATMAN, Columbia, S. C., to Miss Ruby Lee Turner of Winnsboro, June 8.

PAUL JOSEPH KAMINSKI, Chicago, to Miss Dorothy Irene Marlatt of Danville, Ill., in June.

GEORGE V. PAZDRAL, Somerville, Texas, to Miss Lucille Brown at Fort Worth, June 15.

JOSEPH MAY STOWELL, Albany, N. Y., to Miss Jane Grimshaw of Altoona, Pa., June 17.

PAUL C. COLEGROVE, Oberlin, Ohio, to Miss Shirley Fay Burrell at Cleveland, June 16.

JOSEPH EDWARD SEXTON to Miss Loretta Sturdyvin, both of Champaign, Ill., April 19.

TIBOR CZEISLER, Freeport, Ill., to Miss Wanda Murzyn at East Chicago, Ind., in June.

RALPH JUDSON SYKES to Miss Edith Claire Leake, both of Mount Airy, N. C., in June.

EDWARD YOUNG ROSS, Chicago, to Miss Mollie Mildred Luper of Columbus, May 7.

WILLIAM OSCE SELF to Miss Nancy Anderson, both of Ninety-Six, S. C., in June.

JOHN F. KEITHAN to Miss Sara Lavina Deemer, both of Doylestown, Pa., June 10.

THEODORE STUCKART, Dubuque, Iowa, to Miss Edith Thielen of Elkton, S. D., June 14.

WALTER E. CONSTANTINE to Miss Elizabeth Marie Boland, both of Buffalo, June 17.

MARVIN C. MORRIS, Seattle, to Miss Virginia C. Pringle of Muskegon, Mich., July 3.

GORDON VAIL STODDARD to Miss Eva B. Ross, both of East Orange, N. J., May 27.

OLFERT W. TOPP, Charleston, S. C., to Miss Janie McSwain of Greenville, May 13.

HENRY A. SYDOW to Miss Mary Evangeline McGee, both of Omaha, June 6.

ALVIN A. SCHAYE to Miss Henrietta Heftler, both of New York, May 25.

DALE H. DAVIES to Miss Darlene Hansen, both of Omaha, March 25.

Deaths

Walter Drew McCaw ✦ Brigadier General, U. S. Army, retired, Woodstock, N. Y.; Medical College of Virginia, Richmond, 1882; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1884; entered the army as an assistant surgeon in 1884; veteran of the Spanish-American War; received the distinguished service medal for meritorious service during the World War; was on duty in the chief surgeon's office with the American Expeditionary Force, March-October, 1918, and from October, 1918, to July 15, 1919, was chief surgeon in the American Expeditionary Force; chief surgeon, division of the Philippines in 1914 and in 1915 was in command of the Division Hospital at Manila; department surgeon, Southern Department, Fort Sam Houston, Texas, 1916-1917; following service in France was detailed to serve in Washington, D. C., as assistant to the Surgeon General; was retired by operation of law in 1927; at one time was in charge of the library and museum division of the Surgeon General's Office; professor of military hygiene, 1902-1905, professor of military and tropical medicine, 1904-1913, Army Medical School and commandant, 1919-1923; in 1932 was awarded the Silver Star Medal by the United States; received honors from the French, British and Italian governments; honorary member of the Royal Society of Medicine; author of a chapter on "Tropical Surgery" in Keen's Surgery; aged 76; died, July 7.

Robert Verne Day ✦ Los Angeles; University of Southern California College of Medicine, Los Angeles, 1897; member of the House of Delegates of the American Medical Association, 1925-1926; professor of clinical urology at the College of Medical Evangelists; member of the American Urological Association; fellow of the American College of Surgeons; past president of the Western Branch of the American Urological Association, Los Angeles County Medical Association, and the Los Angeles Surgical Society; member of the city board of health, 1903-1904, and city chemist, 1904-1905; served the Los Angeles County Hospital in various capacities; attending urologist to the Cedars of Lebanon Hospital, California Hospital and the White Memorial Hospital; aged 62; died, April 30, of poison self administered.

Laszlo Detre, Washington, D. C.; Magyar Kiralyi Pazmany Petrus Tudomanyegyetem Orvosi Fakultasa, Budapest, Hungary, 1895; member of the Society of American Bacteriologists; special lecturer on allergy, Georgetown University School of Medicine; senior immunologist, division of infectious diseases, U. S. Public Health Service; working independently, he developed a method of detecting syphilis almost identical with the Wassermann test and announced it only two weeks after Wassermann's first publication; aged 64; died, May 26, of tumor of the brain.

Thomas Stewart Blair, Santa Ana, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1889; in 1918 enrolled as a member of the Volunteer Medical Service Corps and served as acting assistant surgeon in the U. S. Public Health Service in the New England states during the influenza epidemic; first chief of the bureau of drug control of the Pennsylvania State Department of Health; for many years on the staff of the Harrisburg (Pa.) Hospital; aged 71; died, April 12.

Elmer Thomas McGaugh, Potter, Ark.; University of Missouri School of Medicine, Columbia, 1899; member of the Missouri State Medical Association; formerly state health commissioner and secretary of the state board of health of Missouri; mayor of Richmond, Mo., 1931-1932; at one time superintendent of the State Hospital, number 1, Fulton, Mo.; aged 66; died, May 5, of acute dilatation of the heart.

John Major Cooley, Kittanning, Pa.; University of the City of New York Medical Department, 1890; member of the House of Delegates of the American Medical Association in 1923; member of the Medical Society of the State of Pennsylvania; past president of the Armstrong County Medical Society; on the staff of the Armstrong County Hospital; aged 73; died, April 21.

George Kissam Meynen ✦ Jamaica, N. Y.; University of the City of New York Medical Department, 1885; fellow of the American College of Surgeons; during the World War served as medical chairman of the local draft board; one of the founders of Jamaica Hospital and its first surgeon; consulting surgeon to the Mary Immaculate Hospital; aged 78; died, April 7.

Lyle Breslau Honeyford, Catskill, N. Y.; Albany (N. Y.) Medical College, 1898; member of the Medical Society of the State of New York; past president of the Greene County Medical Society; formerly member of the board of education; for many years health officer; served during the World War; on the staff of the Memorial Hospital of Greene County; aged 62; died, April 2.

William Clifford McKee ✦ Los Angeles; Johns Hopkins University School of Medicine, Baltimore, 1913; associate clinical professor of obstetrics at the University of Southern California School of Medicine; member of the Pacific Coast Society of Obstetrics and Gynecology; aged 53; on the staff of the Good Samaritan Hospital, where he died, April 21, while visiting patients.

Ernest Llewellyn Bagby ✦ Enid, Okla.; Ensworth Medical College, St. Joseph, Mo., 1898; member of the American Psychiatric Association; medical superintendent of the Northern Oklahoma Hospital; formerly superintendent of the Western Oklahoma State Hospital, Supply; served during the World War; aged 64; died, May 10, of mitral stenosis and myocarditis.

Adelbert David Dye, Helmuth, N. Y.; Hahnemann Medical College and Hospital, Philadelphia, 1905; member of the Medical Society of the State of New York and the American Psychiatric Association; served during the World War; aged 61; died, April 10, of lobar pneumonia and cerebral arteriosclerosis.

Norton George Becker, Kankakee, Ill.; Northwestern University Medical School, Chicago, 1935; member of the Illinois State Medical Society; on the staff of the Kankakee State Hospital; aged 32; died, May 5, in Chicago of subacute endocarditis following a streptococcic infection of the throat.

Alverdi John Simpson ✦ Summerville, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1897; past president of the Jefferson County Medical Society; served during the World War; member of the board of education; aged 70; died, April 9, in the Adrian Hospital, Punxsutawney, of meningitis.

Vincent Gorman Smith ✦ Staten Island, N. Y.; Jefferson Medical College of Philadelphia, 1916; fellow of the American College of Surgeons; served during the World War; on the staffs of the Richmond Borough Hospital, Richmond Memorial Hospital and the Staten Island Hospital; aged 44; died, April 2.

Wilber G. Fish, Ithaca, N. Y.; Cleveland Medical College, 1893; member of the Medical Society of the State of New York; past president and secretary-treasurer of the Tompkins County Medical Society; aged 80; died, April 12, in the Memorial Hospital of prostatitis and nephritis.

Carl Kirby Arnold, Floydada, Texas; Fort Worth School of Medicine, Medical Department of Texas Christian University, 1915; member of the State Medical Association of Texas; served during the World War; aged 48; died, April 30, in a hospital at Plainview.

Joseph B. Carmichael, Duncan, Okla.; University of Georgia Medical Department, Augusta, 1885; member of the Oklahoma State Medical Association; county health officer; on the staff of the Weedn Hospital; aged 74; died April 22, of carcinoma of the prostate.

Parker Benton Stevens, Alstead, N. H.; New York Homeopathic Medical College and Hospital, 1894; formerly president of the school board; on the staff of the Rockingham General Hospital, Bellows Falls, Vt.; aged 70; died, April 19, of coronary thrombosis.

Bransford Louis Adelsberger ✦ Peoria, Ill.; Washington University School of Medicine, St. Louis, 1920; member of the American Urological Association; on the staff of the Methodist Hospital; aged 44; died, May 9, in a hospital at Pekin of a cerebral hemorrhage.

William John Sheehan, Port Chester, N. Y.; Albany (N. Y.) Medical College, 1897; member of the Medical Society of the State of New York; health officer; aged 67; on the staff of the United Hospital, where he died, April 7, of carcinoma of the neck.

William H. Wesley ✦ Pittsburgh; Northwestern University Medical School, Chicago, 1903; formerly instructor in pharmacy at the University of Pittsburgh School of Medicine; on the staff of the Pittsburgh Hospital; aged 63; died, April 5, of pneumonia.

Robert James Grossman, Butler, Pa.; Western Reserve University Medical Department, Cleveland, 1886; member of the Medical Society of the State of Pennsylvania; on the staff of the Butler County Memorial Hospital; aged 80; died, April 22.

Daniel Edward Osborne, St. Helena, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1884; for many years a member of the county board of health; aged 82; died, April 3, in the Victory Hospital, Napa.

Marcus Junger ✠ New York; Uniwersytet Jagielloński Wydzial Lekarski, Cracow, Austria-Hungary, 1899; aged 63; died, April 28, in the Mount Sinai Hospital, of Welch bacterial infection following an operation for kidney stone.

George Diehl Stahley, Gettysburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1875; for many years professor of biology at the Gettysburg College; aged 88; died, April 16, of cerebral embolism.

James E. Hollingsworth, Strang, Okla.; Barnes Medical College, St. Louis, 1902; member of the Oklahoma State Medical Association; aged 68; died April 3, in the Cottage Hospital, Prior, of atrophic cirrhosis of the liver.

George A. Ribenack, Holcombe, Wis.; Rush Medical College, Chicago, 1891; aged 76; died, April 24, in St. Joseph's Hospital, Chippewa Falls, of coronary artery disease, hypertrophy of the prostate and chronic nephritis.

Henry Middleton Fisher, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1875; member of the Medical Society of the State of Pennsylvania; aged 87; died, April 27, of pneumonia.

Edward Jacob Gangloff ✠ Philadelphia; Temple University School of Medicine, Philadelphia, 1918; for many years police surgeon; aged 46; died, April 4, in the Northeastern Hospital of pneumonia.

Henry F. Becker, Danville, Ill.; Missouri Medical College, St. Louis, 1882; member of the Illinois State Medical Society; aged 80; died, May 1, in St. Elizabeth's Hospital of sclerosis of the cerebral vessels.

Edward B. Beeson, Chicago; Hahnemann Medical College and Hospital, Chicago, 1870; aged 91; died, April 11, in the Albert Merritt Billings Hospital of adenoma of the prostate with obstruction.

Anthony Michael Lisena, Jersey City, N. J.; New York Medical College and Flower Hospital, New York, 1936; aged 29; died, April 29, in the Christ Hospital of acute bacterial endocarditis.

Henry Lawrence Fobes, Auburn, Iowa; State University of Iowa College of Medicine, Iowa City, 1897; member of the Iowa State Medical Society; aged 70; died, April 4, of cerebral embolism.

James M. McManus, Menard, Ill.; St. Louis College of Physicians and Surgeons, 1899; managing officer of the Illinois Security Hospital; aged 62; died, April 11, of diabetes mellitus.

Walter C. Beard, Lewisburg, W. Va.; Vanderbilt University School of Medicine, Nashville, Tenn., 1882; aged 80; died, May 27, of hypostatic pneumonia and cerebral arteriosclerosis.

Josephine Z. Walton, Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1901; aged 64; died, April 1, at sea off the coast of South Africa while on a world cruise.

Harry Joseph Frein ✠ Belleville, Ill.; St. Louis University School of Medicine, 1908; on the staff of St. Elizabeth's Hospital; aged 55; died, April 16, of biliary cirrhosis of the liver.

Alfred Herbert Barker, Brooklyn, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1893; aged 79; died, April 25, in Des Moines of carcinoma of the liver.

Everett R. Ulrich, Marine, Ill.; Jenner Medical College, Chicago, 1901; member of the Illinois State Medical Society; aged 60; died, April 11, of acute nephritis following influenza.

Newton H. Barnart, Penns Grove, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1888; bank president; aged 71; died, May 30, of a self-inflicted bullet wound.

James Harry Wilson Anderson, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1906; served during the World War; aged 70; died, April 8, in Greenville, Pa.

Stanley Mountjoy Hall, Moberly, Mo.; Washington University School of Medicine, St. Louis, 1912; aged 53; was found dead, April 18, probably of coronary thrombosis.

John Ballard Tower, Homestead, Fla.; Northwestern University Medical School, Chicago, 1901; member of the Florida Medical Association; aged 65; died, April 13.

William Conyngton, St. Petersburg, Fla.; Columbian University Medical Department, Washington, D. C., 1902; aged 81; died, April 21, of carcinoma of the bladder.

James A. Bates ✠ Camden, Mich.; Medical College of Indiana, Indianapolis, 1892; aged 72; died, May 17, in the University Hospital, Ann Arbor, of meningitis.

Henry Thomas Hodges, Augusta, Ga.; Atlanta Medical College, 1890; aged 79; died, April 7, in the University Hospital of prostatic hypertrophy with obstruction.

George H. Matchette, McPherson, Kan.; American Medical College, St. Louis, 1878; member of the Kansas Medical Society; aged 84; died, April 30, of senility.

Harry Marshall Heald, Buckfield, Maine; Medical School of Maine, Portland, 1897; aged 68; died, April 24, in Lewiston of coronary thrombosis and arteriosclerosis.

Lewis G. Wetterau ✠ McAdoo, Pa.; Medico-Chirurgical College of Philadelphia, 1898; formerly school director; aged 72; died, April 8, of coronary thrombosis.

Philip Gibson Wickens ✠ Rochester, N. Y.; University of Rochester School of Medicine, 1929; aged 35; died, April 12, in New York of gastric hemorrhage.

Henry Herbert Elliott, The Pas, Man., Canada; Queen's University Faculty of Medicine, Kingston, Ont., 1898; aged 66; died, April 24, of chronic myocarditis.

Michael Aloysius Murray ✠ Wilkes-Barre, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1908; aged 71; died, April 3.

George Herman Burfiend, St. Paul; Northwestern University Medical School, Chicago, 1905; aged 60; died, April 6, of coronary sclerosis.

Thomas A. Cohoe, Pilot Mound, Man., Canada; Manitoba Medical College, Winnipeg, 1905; aged 60; died, April 21, of coronary thrombosis.

Charles L. Aldrich, Paris, Maine; Baltimore Medical College, 1901; aged 75; died, April 28, of cerebral hemorrhage and angina pectoris.

Ernest Jackson Hudspeth, Ruleville, Miss.; University of Nashville (Tenn.) Medical Department, 1906; aged 56; died, April 21, of uremia.

Elgin Dorland Vandervoort, Deseronto, Ont., Canada; University of Toronto Faculty of Medicine, 1881; aged 86; died, March 6.

W. J. M. Covington, College Grove, Tenn.; University of Nashville Medical Department, 1876; aged 84; died, April 27, of myocarditis.

Alexis Dupont Smith, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1882; aged 80; died, April 11.

William H. James, Cleveland; Cleveland Homeopathic Medical College, 1898; aged 63; died, April 6, of chronic myocarditis.

Nona Smith Gould, New York; New York Medical College and Hospital for Women, New York, 1915; died, March 15.

Cynthia Agnes McMahan Jones, Lafayette, Ind.; Woman's Medical College, Chicago, 1879; aged 89; died, April 21, of senility.

Frank E. Bullock, Forest City, Mo.; St. Joseph Hospital Medical College, 1881; aged 80; died, April 15, of coronary occlusion.

Gustave A. Lawrence, Milledgeville, Ga.; University of Georgia Medical Department, Augusta, 1892; aged 75; died, April 7.

Colonel Garrad Ellison, Williamsburg, Ky.; Louisville Medical Department, 1885; at one time mayor; aged 77; died, April 9.

Charles Baldwin Langford, Blenheim, Ont., Canada; Victoria University Medical Department, 1888; aged 71; died, April 1.

Lot Bowen Meadows, Normantown, W. Va.; Baltimore University School of Medicine, 1892; aged 73; died, April 22.

Andrew William Dwyre, Perth, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1885; died, April 27.

Frederick Melzer, Milwaukee; Milwaukee Medical College, 1906; aged 68; died, April 10, of carcinoma of the lung.

Charles E. Novak, Humboldt, Neb.; Rush Medical College, Chicago, 1903; aged 59; died, April 25, of heart disease.

A. R. Williams, Aiken, S. C.; Baltimore Medical College, 1892; aged 68; died, March 14, of coronary thrombosis.

J. C. Sumner, Hazard, Ky.; Louisville (Ky.) Medical School, 1893; aged 71; died, April 8, of pneumonia.

John Murray Eaton, Toronto, Ont., Canada; Trinity Medical College, Toronto, 1888; aged 81; died, April 8.

Theophilus H. Gamblin, Monticello, Ky.; Louisville (Ky.) Medical College, 1890; aged 72; died, April 1.

Frederick H. England, Los Angeles; Chicago Physio-Medical College, 1896; aged 83; died, April 8.

Bureau of Investigation

MISBRANDED "PATENT MEDICINES"

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the United States Department of Agriculture

[EDITORIAL NOTE.—The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the composition; (4) the type of nostrum; (5) the reason for the charge of misbranding and (6) the date of issuance of the Notice of Judgment—which is considerably later than the date of the seizure of the product and somewhat later than the conclusion of the case by the Food and Drug Administration.]

Bick's Vapor Salve.—Bick Co., St. Louis. Composition: Essentially small amounts of menthol, camphor, eucalyptol and carbolic acid, in a petrolatum base. Fraudulently represented as an effective treatment for sore throat, catarrh, tonsillitis, bronchitis, rheumatic pains, eczema, etc.—[*N. J. 29041; December 1938.*]

Boro-Septol Tablets.—Boro-Septol Chemical Co., Dallas. Composition: Essentially salt, boric acid and sulfocarbolates of zinc and copper. Not antiseptic when used as directed; fraudulently represented as a remedy for chronic ulcerated conditions, nasal troubles, leukorrhea, cystitis, etc.—[*N. J. 29038; December 1938.*]

Cherokee Iron Tonic.—National Medicine Co., Nashville, Tenn. Composition: Essentially small proportions of compounds of iron, quinine and phosphoric acid, extracts of plant drugs including bloodroot, with glycerin, alcohol and water. Fraudulently represented as a remedy for blood disorders generally and as acting beneficially on the liver and stomach.—[*N. J. 28988; November 1938.*]

Fisher's Columbine Massage Cream.—George B. Fisher, Denver. Composition: Essentially petroleum oil and perfume. Fraudulently represented as a remedy for developing the bust, removing wrinkles, freckles, eczema, scalp diseases, pneumonia, asthma, etc.—[*N. J. 29007; December 1938.*]

Fisher's Massage Liniment.—George B. Fisher, Denver. Composition: Essentially alcohol (8.9 per cent by volume), with water and small amounts of ammonium carbonate and iodides. For "developing the breast and chest . . . for cuts . . . relieves pain . . . beats the world to use in childbirth." Fraudulent therapeutic claims.—[*N. J. 29007; December 1938.*]

Fisher's Pugilitis Pendicitis.—George B. Fisher, Denver. Composition: Essentially water, alcohol, epsom salt and flavoring. For appendicitis, ptomaine poisoning, peritonitis, hay fever, abscesses, female complaints, etc. Fraudulent therapeutic claims.—[*N. J. 29007; December 1938.*]

Ger-Oil.—Ger-Oil Co., Jonestown, Miss. Composition: Essentially a solution or combination of sulfur in turpentine and a saponifiable fixed oil. Fraudulently represented as a remedy for burns, cuts, sores, rheumatic pains, worms in children, "lost manhood," etc.—[*N. J. 29004; December 1938.*]

Herman's (Dr. Joseph) Special Blood Purifier.—E. Freithofer Mfg. Co., Pittsburgh. Composition: Essentially small amounts of an iodide, an iodate, sodium carbonate, and extracts of plant materials, dissolved in water. Fraudulently represented as an effective treatment of stomach ulcers, blood poisons, skin diseases, rheumatism, female complaints, diabetes, etc.—[*N. J. 29006; December 1938.*]

Hi-Test Vaginal Suppositories and Femisan Suppositories.—Respectively labeled Hi-Test Laboratories and Femisan Co., St. Louis. Alleged to be identical products; composition not reported. Falsely represented as a vaginal antiseptic.—[*N. J. 29012; December 1938.*]

I. G. Antiseptic.—Norzel's Beauty Products Mfg. Co., Inc., Syracuse, N. Y. Composition: Essentially water, isopropyl alcohol, glycerin and small amounts of common salt, potassium iodide, sodium carbonate, iodoform and perfume. Fraudulently represented to prevent and eliminate infections, arrest falling hair, remove dandruff, prevent barber's itch, etc.—[*N. J. 29002; December 1938.*]

Kalms.—Seabury, Inc., New York. Composition: Tablets consisting essentially of aminopyrine (2½ grains per tablet), antipyrine and caffeine. For headache, neuralgia, muscular and rheumatic pain, colds, etc. Fraudulent therapeutic claims.—[*N. J. 29008; December 1938.*]

Liberty Castoria.—National Medicine Co., Nashville, Tenn. Composition: Essentially extracts of plant drugs including a laxative drug, with Rochelle salt, baking soda, sugar, alcohol (0.93 per cent by volume) and water, flavored with wintergreen and anise. Fraudulently represented as a remedy for dizziness, stomach and bowel disorders, feverishness, worms, etc.—[*N. J. 28988; November 1938.*]

Liberty Croup and Pneumonia Salve.—National Medicine Co., Nashville, Tenn. Composition: Essentially small amounts of volatile oils including oil of pine, eucalyptol and menthol, in a petrolatum base. Fraudulent therapeutic claims.—[*N. J. 28988; November 1938.*]

Liberty Rheumatic Elixir.—National Medicine Co., Nashville, Tenn. Composition: Essentially sodium salicylate, a small amount of sodium benzoate, alcohol (3.2 per cent by volume), sugar and water. Fraudulent therapeutic claims.—[*N. J. 28988; November 1938.*]

Linoil.—Sutton Laboratories, Inc., Chapel Hill, N. C. Composition: Essentially benzoic and salicylic acids, in an ointment base. Fraudulently represented as a remedy for eczema.—[*N. J. 28996; November 1938.*]

McDonald's Crystalene.—Crystalene Extracts Co., Baltimore. Composition: Essentially alcohol, sugar, water and extracts of plant drugs including nux vomica, licorice and a laxative plant drug. Fraudulently represented as a remedy for biliousness, dyspepsia, dropsy, diabetes, rheumatism, paralysis, etc.—[*N. J. 28995; November 1938.*]

McDonald's Crystalene Laxative Pills.—Crystalene Extracts Co., Baltimore. Composition: Essentially an unnamed laxative plant drug. Fraudulent therapeutic claims.—[*N. J. 28995; November 1938.*]

Myraphen.—Plexo Preparations, Inc., New York. Composition: Small tablets containing aminopyrine (approximately 2 grains each) and caffeine; also, larger tablets containing about 5 grains of aminopyrine, each, and caffeine. For menstrual pains, neuralgia, neuritis, toothache, etc. Fraudulent therapeutic claims.—[*N. J. 29013; December 1938.*]

Na-Sin-Ol.—Na-Sin-Ol Co., Salina, Kan. Composition: Essentially mineral oil, with small amounts of iodine, carbolic acid and camphor. For sinus troubles, hay fever, catarrh, bronchial asthma, earache, etc. Fraudulent therapeutic claims.—[*N. J. 29040; December 1938.*]

National Skin Salve.—National Medicine Co., Nashville, Tenn. Composition: Essentially small amounts of volatile oils, betanaphthol, green soap and a balsam, in a petrolatum base. For eczema, ringworm, tetter and parasitic skin infections. Fraudulent therapeutic claims.—[*N. J. 28988; November 1938.*]

Nonat.—Marie Leiblinger & Co., Altadena, Calif. Composition: Essentially a lead plaster consisting of turpentine, camphor, wax, resin and a lead compound. For carbolic acid burns, splinter wounds, toothache, rheumatism, poison ivy, etc. Fraudulent therapeutic claims.—[*N. J. 28998; November 1938.*]

Nourse Gall Remedy.—Nourse Oil Co., Kansas City, Mo. Composition: Essentially small amounts of a zinc compound and volatile oils including wintergreen and camphor, in a base of petrolatum and lanolin. For "piles," ulcers, boils, skin diseases, etc. Fraudulent therapeutic claims.—[*N. J. 29019; December 1938.*]

Pon-Tam-Pon and Glycerant.—Pond Mfg. Co., Rutland, Vt. Composition: Tampons consisting of gelatin capsules containing a jelly composed of glycerated gelatin, boric acid and an iodide; a layer of powder composed of silver nitrate and boric acid, and a bundle of wool fibers; the Glycerant contained glycerite of starch and boric acid. The combination was fraudulently represented as an effective treatment of gonorrhea in women; the Glycerant, when used separately, was fraudulently represented as an effective treatment for inflammation, skin diseases, hemorrhoids, sore gums, etc.—[*N. J. 29001; December 1938.*]

Q-Loid.—Magay Corporation, New York. Composition: White tablets, 5 grains of aspirin each; yellow tablets, averaging 0.3 grain of sulfur and 0.2 grain of antipyrine, each. Fraudulently represented as a remedy for rheumatic conditions, including arthritis.—[*N. J. 29016; December 1938.*]

Reilly's (Dr.) Herb Tonic.—Thomas I. Reilly, M.D., Boston. Composition: Essentially alcohol, water, extracts of plant drugs including a laxative, and a trace of oil of peppermint. For purifying the blood, destroying systemic germs and poisons, regulating liver and bowels, etc. Fraudulent therapeutic claims.—[*N. J. 29005; December 1938.*]

Reso-Quinon Vaginal Jelly.—White Cross Pharmacals, Inc., Detroit. Composition: Essentially water, glycerin, a gum, boric acid, with small amounts of resorcinol, oxyquinoline sulfate and lactic acid. Fraudulently represented as a remedy for various female disorders.—[*N. J. 29030; December 1938.*]

Sanisalva Salve.—Carnation Co., St. Louis. Composition: Essentially small amounts of menthol, oil of sassafras, camphor and carbolic acid, in a petrolatum base. Fraudulently represented as an antiseptic for cuts, burns, skin diseases, catarrh, etc.—[*N. J. 29041; December 1938.*]

Sunshine Vitamin D Bath Flakes.—Frank J. Peterson, St. Paul. Composition: Essentially a sodium soap containing no therapeutic quantity of vitamin D. Fraudulently represented as a remedy or relief for aches, pains, itching skin, pimples, rheumatism, "athlete's foot," vitamin D deficiency in the system, etc.—[*N. J. 29015; December 1938.*]

Tree of Life Tonic.—Tree of Life Tonic Co., New Orleans. Composition: Essentially water, alcohol and small amounts of salicylates, oil of peppermint and extracts of plant drugs including a laxative. Fraudulently represented as a remedy for stomach, blood, liver and kidney disorders, diabetes, etc.—[*N. J. 29022; December 1938.*]

Valium.—Clematis Laboratories, Waltham, Mass. Composition: Tablets consisting essentially of calcium sulfide, with a red sugar coating. Fraudulently represented as a remedy for varicose veins, varicose ulcers and hemorrhoids.—[*N. J. 28992; November 1938.*]

Vitawine.—Vitawine Co., Miami, Fla. Composition: Essentially water, alcohol (9.8 per cent by volume), citrates, an iron compound, manganese, and a small amount of vitamin B_1. Fraudulently represented as a remedy for colitis, anemia, neuritis, malnutrition, etc.—[*N. J. 29027; December 1938.*]

Correspondence

ANGINA PECTORIS AND CARDIAC INFARCTION FROM TRAUMA

To the Editor:—An article entitled "Angina Pectoris and Cardiac Infarction from Trauma or Unusual Effort" by Dr. E. P. Boas, published in THE JOURNAL May 13, is devoted in large part to the rebuttal of my observation that physical effort is not a factor in precipitating coronary artery occlusion. I have already presented arguments and shall not repeat them; evidence has now been extended to 1,500 cases and will be published elsewhere. My purpose in writing is to correct several beliefs erroneously attributed to me by the author and to point out that some of his conclusions are unwarranted.

The author gives the impression that trauma was excluded as a cause of cardiac damage and symptoms. This is not true; it is universally admitted that trauma can produce contusion of the heart. It is my belief, however, that trauma does not initiate classic coronary occlusion with secondary cardiac infarction clinically, electrocardiographically or pathologically. In the experiments cited by Boas in which the chests of animals were traumatized, postmortem examination showed myocardial and pericardial damage but not coronary artery occlusion.

Another misconception fostered by Dr. Boas is the failure to differentiate between classic coronary occlusion with infarction and cardiac infarction secondary to coronary insufficiency. I did not include the latter in my series, while many of his cases were probably in this group. These two conditions differ clinically and electrocardiographically as well as pathologically, as Büchner has shown, and should be separated completely.

In support of his belief that physical effort may precipitate coronary occlusion, Boas cites thirteen histories of cases observed by him. However, he does not state the incidence of these cases in his entire medical experience of coronary artery occlusion. Being an authority on heart disease and cardiac consultant to the Workmen's Circle, New York, for many years, he has seen hundreds, if not thousands, of patients with coronary artery occlusion among the laboring classes. If effort were a factor in coronary artery occlusion, he should have encountered numerous instances of coronary artery occlusion due to effort and not only twenty-five. Effort is a factor in attacks of angina pectoris, and almost every patient tells of this relationship, but practically never in coronary artery occlusion.

Since Dr. Boas wishes to apply his conclusions to medicolegal cases, he should have omitted the five compensation cases which were among the thirteen he actually cited. The history given by compensation patients is untrustworthy.

The author postulates intimal hemorrhage as the initial mechanism in the formation of coronary artery occlusion and relates it to effort and to a rise in blood pressure. The fallacy of this belief was recently pointed out (Master, A. M.; Dack, Simon, and Jaffe, H. L.: THE JOURNAL, April 22, p. 1620). Intimal hemorrhage is a part of the atherosclerotic process and is independent of external influences. It is found in patients who have been bedridden for weeks or months with cancer, heart failure and the like who give no history of exertion.

In the rare cases of coronary occlusion in which the onset of acute symptoms is associated with effort, it is my belief that the occlusion had been forming or had already formed prior to the exertion. Boas admits that the formation of an occlusion may take place over a period of days. However, once the process has been initiated, effort may bring on pain and other symptoms, although it does not alter the atherosclerotic process. The author saw many of his patients weeks or months after the occlusion; it is probable that, had a careful history been taken at the time of the episode, the presence of symptoms would have been elicited prior to the exertion. I could cite case after case in which coronary occlusion presumably was associated with effort but in which it was possible to prove that the occlusion had occurred several days before, although the patient continued to work. Thus, very recently I was called to see a man 60 years of age who had suffered severe pain during the night following sexual intercourse. His physician had made a diagnosis of acute coronary artery occlusion. Actually, the patient had complained of some substernal pain the week before, and an electrocardiogram taken at that time showed evidence of acute coronary artery occlusion with myocardial infarction, which had not been recognized.

In conclusion, it is evident that the problem of the relation of effort to classic coronary artery occlusion with infarction can be settled only by carefully elicited histories in large numbers of cases, as my associates and I have done in 1,500 cases. Only rarely will there be an apparent association. Yet it should be frequent if effort were a factor, since effort is such a common occurrence in the daily lives of all of us. Furthermore, it is essential to differentiate clearly cases of coronary insufficiency with secondary cardiac infarction from cases of classic coronary artery occlusion, with which I am solely concerned.

ARTHUR M. MASTER, M.D., New York.

SENILE OSTEOPOROSIS

To the Editor:—I have read with great interest your leading editorial on "Senile Osteoporosis" in THE JOURNAL February 4, page 434.

In 1930 I wrote a paper on this subject (Rosenfeld, Wilhelm: Ueber die Forme fruste der Osteomalacie, *Med. Klin.* **26**:421-422 [March 21] 1930). I am happy that other authors have in their own way succeeded in determining this subclinical form of osteomalacia. As therapeutic measures I used chiefly, besides calcium and vitamin D, subcutaneous injections of minimal doses of epinephrine (from 0.05 mg. to 0.1 mg. of epinephrine hydrochloride for each injection), and this remedy proved helpful in my hands. WILHELM ROSENFELD, M.D., Tel-Aviv, Palestine.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SUNTAN OINTMENTS

***To the Editor:*—Will you be so kind as to give me the name and formula of a recommended preparation for promoting suntan?**

Thomas H. Cates, M.D., Tucson, Ariz.

ANSWER.—There are three different types of cosmetic preparations used for exposure of the skin to strong rays of the sun. (*a*) The so-called suntan cream, which permits a tanning of the skin but presumably is designed to minimize the "burn." Such a cream may contain a wool fat as a base with hydrogenated coconut oil and other ingredients. One proprietary form is composed of beeswax, distilled water, hydrous wool fat, borax, zinc oxide, hydrogenated coconut oil, amber petrolatum, color and perfume. (*b*) A cream which is presumed to contain a chemical which will remove the actinic rays of the sun. Such preparations usually contain a substance such as disodium naphthol sulfonate as one of the active ingredients. (*c*) A preparation which stains the skin to produce a tanned appearance. A lotion of such nature generally contains a pigment and sometimes tannic acid as one of its ingredients.

The "promoting" of suntan is a doubtful procedure. There is no officially recommended preparation for such a purpose. The majority of preparations to be used to minimize sunburn depend on the use of substances that are impervious or partially impervious to ultraviolet rays. Many ointments can be used because of the protection rendered by the base or other ingredients. Zinc oxide ointment is quite efficacious, and even boric ointment can be depended on to give some protection. The following formula may be suggested as a safe preparation: calamine 15 Gm., wool fat 10 Gm., petrolatum 40 Gm., rose water to make 100 cc.

FUNGOUS INFECTION OF VAGINA

To the Editor:—**Please discuss the best method of treating vaginitis caused by fungous infections, especially thrush.**

E. M. Ragsdale, M.D., Columbia, Tenn.

ANSWER.—Nearly all vaginal or vulvar discharge due to mycoses or fungi are produced by yeast or yeastlike organisms. These organisms consist of two parts, mycelia and conidia. The mycelia are long fiberlike structures, which are usually branched. The conidia are buds and usually the size of a pus cell but may vary considerably.

When typical fungous infection occurs the vulva is considerably reddened and congested and part of the surface may have a slight grayish cast due to dyeing of the epidermis. Since in nearly all cases there is considerable itching, the vulva may show excoriations from scratching. The vaginal wall and introitus are usually covered with tenacious, caseous material which resembles thrush in the mouth of newborn babies. In fact, as shown by Plass and Hesseltine, the two organisms are identical. The walls of the vagina are intensely congested.

The diagnosis of mycotic infections is made most simply by making a hanging drop examination or by taking a smear of a small portion of caseous material and staining for the fungi.

The treatment of yeast infections is generally simple. The thorough application to all parts of the vulva and vagina of a 1 to 5 per cent aqueous crystal violet or gentian violet solution nearly always gives spectacular and gratifying relief. This treatment should be carried out every day or every second day for four or five times or until a cure is accomplished. The patient must be warned that the dyes stain the clothing and that sufficient vulvar pads should be worn at all times. Karnaky advocates a solution of 5 per cent gentian violet in 40 per cent ethyl alcohol, and Hesseltine recommends element iodine as found in one-half to one-fourth strength compound solution of iodine or one-fourth to one-fifth strength tincture of iodine (aqueous dilution).

Shelanski and Kern state that moniliasis will respond to treatment with silver picrate as effectively as to gentian violet without the disadvantage of intense staining. With this method the vagina is cleansed with a cotton sponge saturated with a suspension of kaolin in aluminum hydroxide, rinsed with sterile water and dried. The vagina is then painted with a 1 per cent aqueous solution of silver picrate, and 5 Gm. of 1 per cent silver picrate in kaolin is insufflated into the vagina. These treatments are repeated at weekly intervals.

BLOOD DONORS

To the Editor:—**I am the chairman of the local chapter of the Red Cross and have been asked about the advisability of establishing a group of certified blood donors here. Under whose auspices are such lists kept up in most communities? It would seem to me to be a hospital function rather than that of the Red Cross. How often must Wassermann tests be done on donors on such a list? The local Y. M. C. A. man receives many requests for blood donors and has many men willing to give blood, but they are not typed. How is this situation usually handled?**

Charles F. Walcott, M.D., Cambridge, Mass.

ANSWER.—The answers to most of these questions can be found in the article by Philip Levine and E. M. Katzin (A Survey of Blood Transfusion in America, THE JOURNAL, April 16, 1938, p. 1243). In the United States different institutions employ various sources for their blood donors. Many hospitals have their own lists, usually consisting mainly of employees; others use donors from commercial agencies and still others use donors from their own lists and employ commercial donors as well. In a few cities noncommercial donor agencies are operated by the local board of health or are under the auspices of the county medical society. A number of organizations, such as the American Legion, the police and fire departments and certain utility companies, maintain their own lists of volunteers compiled from their membership, so that if any employee is injured another can act as a blood donor for him. Finally, of course, when volunteer donors are not available and the patient cannot afford to pay for a certified blood donor, friends or relatives of the patient may be examined and act as the blood donor.

Several chapters of the Red Cross, notably in Augusta, Ga., Baltimore, Md., and Paterson, N. J., have organized blood donor services. Apparently, however, no further promotional work is being undertaken in this activity until a careful analysis of those services already organized has been completed. In London, however, the British Red Cross organized a volunteer blood transfusion service in 1921, and a similar transfusion service is operated by the Red Cross in Rotterdam. These Red Cross transfusion services have done excellent work, making possible thousands of transfusions each year which might otherwise be out of the question. Donors in the service are forbidden to receive any remuneration, and the patient's identity is kept secret from them. In the Netherlands each donor is given a medal bearing the likeness of Dr. Karl Landsteiner, discoverer of the blood groups, as a memento of his service.

With regard to Wassermann tests, the practice in different communities varies, the intervals between examinations varying from one to six months. The best procedure is to have such tests done shortly before the transfusion. Many hospitals perform a test immediately before a transfusion and for this purpose employ some rapid procedure such as the Kahn or Kline test.

Men who wish to volunteer as blood donors must of course have their blood grouped and must also be subjected to a physical examination, including a hemoglobin determination. Naturally, for this work one or more physicians are required, and if none are available to the Y. M. C. A. in your community it would be advisable to consult with the local county medical society.

BLOOD PRESSURE AND OBESE ARM

To the Editor:—**Obviously more pressure is required to shut off the circulation in a thick, fat arm than in a thin one. Can you tell me what approximately would be the difference in systolic pressure in two patients, one 64 inches (163 cm.) tall and weighing 240 pounds (109 Kg.), the other being the same height and weighing 125 pounds (56.7 Kg.)? I mean, of course, the difference due to thickness of the tissues only, with all other conditions the same. I never have happened to see this discussed, though no doubt it has been many times.**

B. A. Higgins, M.D., Sylvan Grove, Kan.

ANSWER.—The inquirer probably confuses the systolic pressure with the sphygmomanometer reading. The reading is not greatly distorted by the thickness of the arm if the usual wide (12 cm.) compression cuff is employed. With the broad cuff an error of about 5 per cent arises. Use of a narrow constrictor, however, may introduce an error up to about 40 per cent. The importance of the width of the cuff was first pointed out by von Recklinghausen (*Arch. f. Path. u. Pharmakol.* **46**:78, 1901). The narrow band must overcome the oblique tension of the compressed tissue as well as the internal pressure of the vessels or true arterial tension. With a wide cuff this additional resistance exists only at the edge of the cuff and is therefore a much smaller fraction of the total compressive force (Norris, G. W.; Bazett, H. C., and McMillan T. M.: Blood Pressure, Philadelphia, Lea & Febiger, 1927, pp. 85-87).

There are other sources of error in blood pressure determinations that are much more significant. The most common distortion arises from psychic stimulation of the patient. Prolonged constriction of the arm is a frequent source of error in examinations by the inexperienced. Prolonged constriction may be most uncomfortable. This is especially conspicuous with obese persons. Comparisons of readings obtained by rapid cuff inflation and deflation with those observed when constriction is prolonged reveals that continued compression may elevate the tension as much as from 20 to 40 mm. of mercury. Several rapid observations give more accurate readings (Erlanger, J.: *Am. J. Physiol.* **40**:82 [March] 1916).

ROCKY MOUNTAIN SPOTTED FEVER

To the Editor:—**Kindly advise me whether it is a vaccine or a serum that is used for prophylaxis of the Rocky Mountain spotted fever carried by the wood tick. I would also like to know whether it is advisable to give it to my child before he goes to camp for the summer and how and where I can obtain it.**

Clinton S. Herrman, M.D., Philadelphia.

ANSWER.—The material used as a prophylaxis against Rocky Mountain spotted fever is a vaccine. No serum of therapeutic value has yet been developed nor is the vaccine effective as a cure.

Over a period of fifteen years the usefulness of the Spencer-Parker vaccine as a preventive and in the reduction of the fatality rate (some vaccinated persons may suffer from mild attacks) has been established beyond doubt. The duration of the protection conferred varies a great deal with the individual.

The vaccine is prepared only by the United States Public Health Service at its Rocky Mountain Laboratory, Hamilton, Mont. It is expensive to make and a limited supply is kept on hand at this station and at the National Institute of Health, Washington, D. C. Since there are less than 1,000 cases in the United States each year, mass vaccination is not practical. In certain locations in which the disease is endemic vaccination is extensively employed.

The best prophylaxis is to stay away from tick infested areas. A pamphlet describing ways and means of preventing tick bites for those whose occupations necessitate exposure may be secured at Hamilton, Mont., or Washington, D. C. Small quantities of the vaccine are issued to physicians on request.

MENTAL AND PHYSICAL RETARDATION

To the Editor:—A white girl aged 15 has shown slow growth and some mental retardation since the age of 6 years (she is now three years behind in school). The past history reveals a normal birth, with a birth weight of 6 pounds (2,722 Gm.). There was slight jaundice the first few days. The first teeth appeared at about 1 year. She walked and talked at 21 months. The patient had pyelitis at 13 months and again at about 20 months, and to this has been attributed the slow development. She had measles at 3 years and pertussis at 5; otherwise the past history is negative. There is no family history of glandular dyscrasias. An older sister (aged 19) is normally developed physically and mentally. At the aged of 6 years, while in Europe, the patient was advised to take thyroid and she has been taking it intermittently ever since. The mother reports that there was considerable improvement in the child's growth and mental attitude, loss of "pot belly" and an improvement in the texture of the skin and hair following thyroid medication. From the age of 8 to 12 the child attended a clinic, where the thyroid was continued. X-ray examinations of the sella turcica were negative. An intelligence test showed a dull normal in 1936. Repeated tests in 1938 showed an intelligence quotient of 90. From Feb. 27 through May 12, 1937, the patient was given sixteen injections of antuitrin-G, a growth promoting principle derived from the anterior pituitary, by another physician, who also prescribed pituitary, pineal and thyroid extracts by mouth. Before injection the height was 50¾ inches (129 cm.), weight 64 pounds (29 Kg.); at termination the height was 51½ inches (131 cm.), weight 67¼ pounds (30.6 Kg.). During the next few months, however, growth was a little more rapid. Jan. 18, 1939, she reached a height of 54 inches (137 cm.). The total gain in height for that year was 3¼ inches (8.26 cm.). When I saw her January 28, the mother's principal concern was absence of any signs of sexual development. The child had not menstruated as yet and there was no pubic or axillary hair. The patient was fairly alert and looked about 10 or 11 years of age. *The body is symmetrical. The skin* and hair are dry but not coarse. There is absence of pubic and axillary hair. The height is 54 inches, the weight 72½ pounds (32.8 Kg.). The span is 52¾ inches (134 cm.). The heart and lungs are normal; the pulse is 80. The results of laboratory examinations are as follows: 1. X-ray films of the wrists showed normal bone development; the epiphyses of the long bones were not closed. 2. The basal metabolic rate was —7 (with thyroid medication of one-fourth grain three times a day). 3. The blood cholesterol was 268 mg. Kindly advise whether this is a case of hypothyroidism per se or whether possibly other glands are involved. Would further use of antuitrin-G be of any value? What is the prognosis as to her ultimate size and sexual development? M.D., New York.

ANSWER.—The data are inadequate for an accurate diagnosis, particularly those relating to her early development. If the blood cholesterol is correct, the patient is apparently receiving an inadequate dose of thyroid. It would be desirable to give the patient 1 grain (0.065 Gm.) of U. S. P. thyroid daily (from 0.18 to 0.23 per cent iodine) and if improvement is not satisfactory this might be increased to 1½ grains (0.1 Gm.) daily at the end of three months. If after six months the patient has grown but little, stimulating genital development with pituitary gonadotropic factor (300 units per cubic centimeter) in a dose of 1 cc. daily for twenty-one days might be tried, following with other similar courses of treatment after a rest period of twenty-one days. This should be given in addition to the thyroid. Stimulation of sexual development may produce some stimulation of skeletal development. If the patient has primary hypothyroidism, her condition can be relieved as much as it is possible to relieve it by thyroid alone. Failure to show improvement with the proper dose of thyroid means that other factors are involved. Little improvement is to be expected in her mental development beyond that associated with increased experience. On the other hand, considerable skeletal growth may still occur.

TREATMENT OF OSTEOCHONDRITIS DEFORMANS COXAE JUVENILIS

To the Editor:—What is the most recent information on the medicinal, dietary and other therapeutic measures used in the treatment of Perthes' disease? E. C. Hanisch, M.D., St. Paul, Neb.

ANSWER.—The condition referred to should be called Legg-Calvé-Perthes' lesion or osteochondritis deformans coxae juvenilis or coxa plana. Osteochondritis of the hip is a self-limited disease. It should be treated by recumbency in bed with abduction traction of the leg for from five to ten days, then the application of a plaster of paris spica and later a brace. Calot manipulates the hip as in cases of congenital dislocation and applies a plaster of paris cast. Phemister, Kidner and others have operated for this condition. Whitman performed his reconstruction operation with success in arrested cases.

General treatment includes reduction of weight if necessary, removal of foci of infection, proper food, good hygiene, viosterol, cod liver oil, calcium, phosphorus and heliotherapy. The indications are relief from weight bearing, relief from the effects of gravity and relief of muscle spasm. The methods of meeting these indications are absolute and prolonged rest in bed; application of leg traction for from five to ten days (straight at first, abduction later); application of a plaster spica from the toes to the margin of the ribs for from one to two months; use of crutches; construction of block under the shoe of the opposite side, removal of the cast and making of a model for brace (removable plaster, celluloid spica, Taylor traction hip brace, Thomas hip splint, Bradford abduction hip splint), after from two to four months discarding of braces and use of crutches and shoe block only, and maintenance of nutrition of the entire body by massage of every part except the affected hip region. Operation is rarely indicated. Recent reports, especially from Danforth and foreign authorities, indicate that restoration of the form as well as the function can be accomplished by years of non-weight bearing. Danforth concluded that absence of weight bearing is the essential factor. Movement is not, as a rule, detrimental and may possibly be of importance in maintaining the nutrition of the surrounding tissues and possibly of the epiphysis as well. On the theory that the changes in the femoral head and neck in coxa plana were brought about by a disturbance in the circulation of the epiphysis secondary to the inflammatory changes of the soft tissue, and because healing in coxa plana is sometimes associated with deformity and is usually quite prolonged, owing to the residual scarring and poor circulation, Ferguson and Howorth devised an operation for the revascularization of the femoral head. The hip is exposed through a Smith-Petersen incision and the capsule is incised anteriorly. The hip is then inspected and specimens of synovial membrane and capsule are taken. A small window is cut in the cortex of the femoral neck proximally (the bone and periosteum are retained for the laboratory). Through the opening, several holes are drilled with curved awls and curets into the femoral head in various directions. The opening is closed with a bit of muscle to prevent bleeding into the joint. Careful hemostasis and anatomic closure are made, and a snug adhesive strapping and flannel spica are applied. Ferguson and Howorth found that in the active stage drilling of the femoral head for revascularization halted the advance of the process and resulted in earlier and more complete repair. In the reparative stage, when activity has completely subsided, no treatment is usually indicated. In the residual stage, subtrochanteric osteotomy or arthroplasty may be desirable in selected cases. Degenerative arthritis has been a sequel in some cases. The medicinal treatment includes chiefly the glandular extracts which are indicated in certain of the cases: thyroid in some, pituitary in others and ovarian extract in some cases. Roberts advocated the use of mercury and the iodides.

FERTILIZATION OF OVUM WITHOUT SPERMATOZOA

To the Editor:—In the March 20, 1939, issue of *Life*, page 59, showing photographs under the title "Fatherless Bunnies Are Born to Virgin Rabbit," there is a picture of a black rabbit adult from an ovum allegedly fertilized with heat and not with sperm. Do you feel that there has been an error of technic and has this world, which is so rapidly changing, produced another assault on mother nature? What is the true biologic opinion here? I do not recall an asexual cycle in multicellular animals. M.D., Louisana.

ANSWER.—More than thirty years ago Jacques Loeb demonstrated that eggs of such invertebrates as starfish or sea urchins could be stimulated artificially (without the use of spermatozoa) and that these would develop into swimming larvae quite indistinguishable from normal larvae produced through fertilization of the egg. Bile salts, heat, mechanical agitation, organic acids or hypertonic solutions were all capable of initiating some development in the egg. Certain invertebrates reproduce normally without fertilization, and, in the case of bees, the male always arises from an unfertilized egg whereas eggs that are fertilized by spermatozoa develop into females.

Among the vertebrates various amphibia (frogs, newts) have been successfully developed without normal fertilization; eggs have been stimulated by various means to develop into larvae, and some have metamorphosed. Eggs from which the nucleus has been extirpated have been fertilized with spermatozoa, and larvae arising have passed metamorphosis into the adult type.

Among mammals, Dr. Gregory Pincus of Harvard has reported for the rabbit that eggs removed from the oviducts and mixed with spermatozoa in a dish can be successfully fertilized and returned to the tubes of another rabbit and complete their development and birth within the normal limits of time. It has also been claimed that unfertilized eggs removed from the oviduct can be stimulated to develop to some extent. No scientific account in which claims are made that such artificially stimulated eggs of the rabbit, reintroduced into the oviducts, have gone sufficiently far in development as to produce living young has been seen. Such an attainment, however, seems entirely possible on the basis of the known facts.

POSSIBLE OVARIAN CYST

To the Editor:—A girl, said always to have been healthy and strong, began to menstruate normally at 11; at 13 the abdomen was aspirated and from 7 to 8 quarts of fluid was removed. She was well for a year and then signs and symptoms of the abdominal trouble began and at 15 some one made six attempts to aspirate without obtaining a drop, although signs of fluid were marked and the distress was considerable. Within a week the distention lessened rapidly and she was "normal" for a year. The signs and symptoms then began to recur, and after another year, when she was 17, she was tapped of 4 gallons of a watery appearing fluid that showed no albumin and was microscopically negative. A guinea pig injection was negative. I have thought of tuberculous, peritonitis, portal obstruction (no enlargement of the liver or of the spleen), and ovarian cyst adherent to the anterior part of the abdomen but I can't understand the watery fluid that is reported "negative." After a month, I plan an exploratory laparotomy after she has had a chance to recover her normal balance, but I need your suggestion. The girl is not underweight, is seemingly strong and has only this gradual accumulation, which has caused an increasing pressure for a year. I can't understand why fluid absorbed at 15 with a dry tap, although she did increase the output of urine.

M.D., New Jersey.

ANSWER.—It is difficult to arrive at a definite diagnosis from the history as given. It is probable that the young girl may have a large ovarian cyst which was aspirated successfully the first time. During the second attempt the cyst may have been partially ruptured by the repeated attempts at aspiration and the fluid may have escaped into the peritoneal cavity, where it was slowly absorbed. It was possible to aspirate the cyst successfully again at the most recent attempt, for it had slowly refilled. Serous cystadenomas of the ovary reach fairly large sizes and accumulate fluid slowly. They are benign in character. A laparotomy is justifiable in this case.

FIXATION OF DIAPHRAGM AFTER ACCIDENT

To the Editor:—A man aged 50, a city fireman, suffered injuries in the cervical region in an automobile accident five months ago. X-ray examinations were negative. A short time afterward a pain developed in the left side anteriorly on the lower border of the ribs. Fluoroscopically he shows fixation and elevation of the left leaf of the diaphragm. His heart is rotated to the right. An electrocardiogram shows some myocardial degeneration. Have you reports on similar cases or can you give me any references? May this be due to an injury to the cervical plexus involving the phrenic nerve or is it a congenital condition?

M.D., N. Y.

ANSWER.—It seems improbable that the man is suffering from an injury to the phrenic nerve because he should have had symptoms of diaphragmatic involvement immediately after the accident. In addition, it appears unreasonable to assume that the automobile accident singled out the third and fourth cervical nerves only on one side. This may be a case of congenital diaphragmatic hernia arising from imperfect development of one or both halves of the diaphragm. This condition is most common on the left side.

OPTIC ATROPHY AND LIGATION OF COMMON CAROTID

To the Editor:—A man aged 47, a common laborer, suffered an incised wound of the right cervical region Dec. 7, 1938. About Jan. 9, 1939, a diagnosis of traumatic aneurysm of the right carotid artery was made. On January 19, the patient was operated on and an aneurysmal sac of the internal carotid which communicated with the internal jugular vein was resected. Due to postoperative hemorrhage it was necessary to ligate the common carotid artery. On April 6 the patient was examined by an eye specialist, who found post-papillitic optic atrophy on the right side and optic neuritis on the left side. The blood and spinal fluid examinations show a negative Wassermann reaction. Apparently there are no mental changes. Will you please let me know if you think there is a definite causal relation between the accident and the optic changes.

Pablo G. Curbelo, M.D., San Juan, P. R.

ANSWER.—From the data presented a definite answer to the question cannot be given. One would like to know, for instance, whether the internal jugular vein was also ligated at the time of the resection of the aneurysm and the definite ligation of the common carotid artery. Secondly, it is important to know the patient's visual acuity, which is not mentioned, and also whether there is loss of vision in one or both eyes and, if there is, whether it occurred directly after the operation January 19. In the third place, the condition of the optic fundi is not clearly stated. Is the optic atrophy on the right side primary optic atrophy secondary to choked disk, or the result of a thrombosis of the central artery?

If one may assume that the optic atrophy on the right is due to thrombosis and that loss of vision occurred immediately after the operation, there would be a causal connection between the operation and the loss of vision. It would be assumed in this case that a thrombosis at the site of the operation was transmitted to the central artery of the eye. The diagnosis would rest on rapid loss of vision plus changes in the arteries of the retina as viewed by the ophthalmoscope. On the other hand, if there was interference of the venous return from the skull due to ligation of the internal jugular vein, bilateral optic atrophy with choked disk might well follow. It would be unusual, however, for one optic nerve to reach a stage of secondary optic atrophy as rapidly as is indicated by the sequence of events.

Finally, primary optic atrophy on the right side with choked disk on the left side is suggestive of pressure on the right optic nerve, usually the result of neoplasm. The syndrome is known as the Foster Kennedy syndrome and is not related, so far as is known, to interruption of circulation in the common carotid artery or the internal jugular vein. Here again pressure of the spinal fluid, if increased, would be a valuable sign, as well as would the amount of protein in the cerebrospinal fluid.

MANIC-DEPRESSIVE PSYCHOSIS AND MENSTRUAL CHANGE

To the Editor:—A married woman aged 26 is the mother of one child aged 4 years. Approximately eight months ago her menses were reduced from four to one day periods and associated with this change was the development of a psychosis, apparently of the manic-depressive type. The peculiar thing about this phenomenon is the fact that the periods of most marked depression invariably come at the exact midmenstrual point and continue for approximately ten to fourteen days, when there is a practically complete remission for another ten to fourteen days. Although this patient has not been seen by a psychiatrist, I am of the opinion that the problem is not one of hysteria. The patient's domestic life is happy and she has no obvious source of worry. Her physical examination and all laboratory procedures are essentially negative. She has a pilonidal cyst. I should appreciate some word as to the frequency of such psychoses coming on in this cyclic fashion, with the onset of ovulation, and such recommendations as you may have for endocrine therapy.

M.D., Illinois.

ANSWER.—It is not mentioned whether the patient is in a manic state or in a depressed phase. In depressed phases one frequently sees changes or alterations in the menstrual periods. The most common alteration is a marked diminution in the quantity of the flow and then a decrease in the duration of the flow. As is well known, manic-depressive psychoses are also called cyclic or circular psychoses. The latter names have no designation of a relationship to the menses or to ovulation. This patient apparently continues to remain involved with periods of apparent improvement. This is a common observation in all cases of manic-depressive insanity. At the present time most investigators feel that the menses have no active relationship as an etiologic factor in manic depressive psychoses. Theelin and its related substances have had some success in cases of depression (involutional).

PETROLATUM AND HIRSUTISM

To the Editor:—I am using plain petrolatum on my face. I have a difficult skin and I find that the old fashioned yellow petrolatum keeps it in better condition than any cold cream. Will it grow hair? Is it in any way harmful?

M.D., California.

ANSWER.—No application to the skin that is known has the capacity either to increase or to retard the growth of hair. There is a commonly mistaken impression that certain creams are conducive to the growth of hair of some women's faces. This probably arises from the fact that many women become more concerned with the creams they use about the time the skin begins to show signs of aging. At this time, too, most women have an increased growth of facial hair. They often conclude, therefore, that the creams on which they have focused their attention gave rise to the concomitant increase of facial hair. Neither petrolatum nor cold cream of themselves will cause growth of hair. In certain types of skin with acne, the use of creams is contraindicated. It is probable that petrolatum also may aggravate some cases of acne already established.

PULMONARY TUBERCULOSIS AND SULFANILAMIDE

To the Editor:—Will you kindly give me information on the use of sulfanilamide in the treatment of pulmonary tuberculosis?

M.D., Oklahoma.

ANSWER.—There are several experimental observations already published (Rich, A. R., and Follis, R. H., Jr.: *Bull. Johns Hopkins Hosp.* **62**:77 [Jan.] 1938; Smithburn, K. C.: *Proc. Soc. Exper. Biol. & Med.* **38**:574 [May] 1938; Greey, P. H.; Campbell, H. H., and Culley, A. W., *ibid.* **39**:22 [Oct.] 1938; Buttle, G. A. H., and Parish, H. J.: *Brit. M. J.* **2**:776 [Oct. 15] 1938) which show that intensive treatment with sulfanilamide alters the evolution of experimental tuberculosis

in guinea pigs. It has been the experience of certain observers, however, that the drug is not highly effective in the treatment of moderately advanced or advanced pulmonary tuberculosis. Hence it would seem best at the present time to use the drug only under the most carefully controlled conditions for the treatment of tuberculosis in human beings. It should be understood that the use of the drug for this purpose is in a highly experimental stage.

ARTERIAL OCCLUSION IN ARMS

To the Editor:—**A woman aged 52 apparently had occluded brachial and radial arteries on both sides. In 1932 the patient had been observed in the hospital. She then complained of arthritic pains in the hands and back. Pulse and blood pressure readings were noted. In 1937 a note was made in her record that the pulse could be felt only faintly at the wrist and that blood pressure readings could not be obtained over the brachial arteries. Her Wassermann reaction was negative. X-ray examination of the arm showed the outline of the brachial and radial arteries but no calcification. X-ray examination of her chest was negative. Her fundi were not noteworthy. Good pulsation was felt in both dorsalis pedis arteries, and the blood pressure then was about 180. The process was taken to be arteriosclerotic. I would appreciate greatly any references to similar cases that you might be able to give me. I may say that her symptoms in the hands at the present time are coldness, brittleness of the nails and advanced rheumatoid arthritis. Provided the environment is comfortably warm, her hands show a skin temperature of about 31 C. (87.8 F.) and a response of about a degree to immersion of the legs in warm water. A tourniquet causes fair filling of the veins.**

M.D., Canada.

ANSWER.—The most likely cause of the arterial occlusion is arteriosclerosis obliterans, although such a condition is comparatively rare in the upper extremities only. The occlusion may be due to localized atheroma at the origins of the subclavian arteries. Calcification of arteries which is visible in a roentgenogram is not always present in arteriosclerosis obliterans. The differential diagnosis should include cervical ribs, the scalenus syndrome, acral scleroderma and embolic arterial occlusion as the result of heart disease. In general, occlusive arterial disease of the upper extremities is much less serious than similar involvement of the lower extremities, and gangrene occurs less often. In the case mentioned, the good response of skin temperature would indicate that the collateral circulation is adequate and that the arterial blood supply of the hands is fairly good.

FOOD BEFORE SWIMMING

To the Editor:—**The director of a summer camp asked me whether it would be injurious or dangerous to allow swimmers two graham crackers and a glass of milk from fifteen minutes to half an hour before swimming. Since I did not feel qualified to answer this question, I am writing to you for your opinion.**

P. B. Monroe, M.D., Two Harbors, Minn.

ANSWER.—Under the conditions specified there should be no objection to this amount of food one half hour before swimming, provided the subjects are in a good state of health. From a physiologic point of view, however, the margin of safety is unavoidably reduced, so that if there is any tendency to cramps there would be proportionately more danger In the digestive state the blood that would normally be concentrated in the digestive organs is partly diverted to the muscles when the latter become active in any exercise. However, the diversion is not complete enough to supply the muscles adequately; consequently neither these nor the digestive organs are adequately supplied. Exercise in cool water thus imposes a demand which may result in cramped muscles with attendant dangers. The demand imposed by the small amount of food specified should not, however, be of severe consequence.

BRITTLE, SPLITTING NAILS

To the Editor:—**Can you tell me the cause of dryness and splitting of the nails? The case in mind is one in which the nails become dry, develop a ridge and then split at the ends. What is the cause of this condition and the treatment or cure?**

M.D., Texas.

ANSWER.—The causes of brittle or reedy nails are manifold. Frequent washing with soap and water or occupations which require prolonged use of soap and water may be at fault. The use of nail polishes and glazes and their removal with such solvents as acetone remove the natural oil from the nails, drying them. Any local irritation of the skin in the vicinity of the nails and nail beds which may reach the nail matrix can distort the nails and change their consistency, making them less flexible. Invasion of the nails by fungi may make them friable and crumbly. Systemic disorders too may cause the nails to be dry and easily split; these include, among others, hypothyroidism, hyperthyroidism and gout. The nails not infrequently become reedy in old age.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, July 22, page 355.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Sept. 11-13. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th Street, Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. *Written.* Various places throughout the United States, Sept. 9. *Oral.* Part II. Philadelphia, Oct. 14-15. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written.* Various large cities in the country, Oct. 9. *Applications must be received by the Secretary by Sept. 1. Oral.* Philadelphia, Nov. 3-4. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Various sections of the United States, Oct. 16 and Feb. 19. Formal application must be received before Aug. 20 for the Oct. examination and on or before Jan. 1 for the Feb. examination. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written examination and review of case histories (Part I) for Group B candidates* will be held in various cities of the United States and Canada, Dec. 2. *Applications for admission to Group B, Part I, examinations must be on file not later than Oct. 4. General oral and pathological examinations (Part II) for all candidates (Groups A and B)* will be conducted in Atlantic City, N. J., June 6-8. *Applications for admission to Group A, Part II examinations must be* on file not later than March 15. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* March 9. Formal application must be received before January 1. *Oral.* Chicago, Oct. 7 and New York, June 10. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Boston, January. *Applications must be filed on or before Nov. 1.* Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 6-7. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: Memphis, Nov. 22-23. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: New York, April 30 and May 1. Kansas City, Mo., preceding the Region III meeting of the American Academy of Pediatrics. Seattle, preceding the Region IV meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, December. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Atlanta, Ga., Dec. 9-11. Sec., Dr. Byrl R. Kirklin, 102-110 Second Avenue S.W., Rochester, Minnesota.

AMERICAN BOARD OF SURGERY: *Part I (Written).* Simultaneously in various centers throughout the United States, Oct. 9. *Applications must be received by the Secretary not later than Aug. 15.* Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

Arkansas June Examination

Dr. D. L. Owens, secretary, State Medical Board of the Arkansas Medical Society, reports the written examination held at Little Rock, June 8-9, 1939. The examination covered twelve subjects. An average of 75 per cent was required to pass. Sixty-six candidates were examined, all of whom passed. The following school was represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine		(1937)	87.8, 90.9, (1938) 84.3, (1939) 82.2, 82.7, 83.3, 84.4, 84.5, 84.6, 84.8, 84.8, 84.9, 85.3, 85.4, 85.5, 85.8, 86.3, 86.4, 86.5, 86.6, 86.7, 86.9, 87, 87, 87.2, 87.3, 87.5, 87.6, 87.8, 87.8, 87.8, 87.9, 87.9, 88, 88.2, 88.3, 88.5, 88.5, 88.8, 89, 89.1, 89.2, 89.3, 89.3, 89.3, 89.3, 89.3, 89.4, 89.4, 89.6, 89.9, 90, 90.2, 90.4, 90.5, 90.7, 90.7, 90.8, 90.8, 90.9, 91, 91.1, 91.2, 91.3, 91.3, 91.8

Thirteen physicians were licensed by reciprocity and one physician was licensed by endorsement from January 18 through June 8. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Atlanta Medical College, Emory University		(1915)	Georgia
Loyola University School of Medicine		(1926)	Illinois
Tulane University of Louisiana School of Medicine		(1937), (1938)	Louisiana
Ensworth Medical College, Missouri		(1909)	Oklahoma
Washington University School of Medicine		(1920), (1933)	Missouri
Jefferson Medical College of Philadelphia		(1929)	W. Virginia
University of Pennsylvania School of Medicine		(1925)	Mississippi
Meharry Medical College		(1938)	Tennessee
University of Tennessee College of Medicine		(1935), (1936)	Tennessee
University of Virginia Department of Medicine		(1929)	New York

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Washington University School of Medicine		(1937)	N. B. M. Ex.

Book Notices

A Manual of Fractures and Dislocations. By Barbara Bartlett Stimson, A.B., M.D., Med.Sc.D., Associate in Surgery in the College of Physicians and Surgeons, Columbia University, New York City. Fabrikoid. Price, $2.75. Pp. 214, with 95 illustrations. Philadelphia: Lea & Febiger, 1939.

It is not difficult to pick out the best parts of this manual on fractures and dislocations and praise this maiden effort of the author. The diction is excellent, the printing all that could be asked and the format handy and convenient. In the text the discussions of fractures and dislocations about the elbow are very well covered; one wishes that equal attention and space had been allotted the all important fractures of the neck and shaft of the femur and the frequent injuries to the other bones of the leg. Even for undergraduate purposes these are far too scantily covered, as fractures of these bones occur most frequently and cause the highest percentage of disability and economic loss the country over. The reason for this discrepancy may lie in the author's explanation of her service in a hospital which treats a high proportion of ambulatory victims of fractures. Strangely, the stirrup cast for the leg, now in general use, is not described or illustrated. The illustrations seem amateurish and some quite misleading; in fact, figure 2, doubling later as figure 82, might better have been left out, with its apparent constriction about the popliteal space and lack of the pillow support insisted on as an essential factor by Russell. In the present era of teaching by visual methods, bone displacements in fractures should be copied with exactness, and methods of splinting or traction, which may be shown with clearness by faithful line drawings, should give detailed information to the reader. Too frequently the student recalls the picture much better than the written text. May this small volume add another stone in the arch of fracture treatment.

Brazilian Medical Contributions. Paper. Pp. 181, with illustrations. Rio de Janeiro: Livraria José Olympio—Editora, 1939.

The author reviews the most important practical achievements and research work contributed by Brazilian physicians. Brazilian civilization began with the arrival of Don John VI, king of Portugal, who brought with him scientists from the University of Coimbra in the seventeenth century. The first school of medicine in Brazil was founded in Bahia in 1815. The Bacteriologic Institute of São Paulo began its work in 1890 after the yellow fever epidemic of the previous year. Pasteur of Paris was requested to choose the director, and he named Dantec. Dantec's health, however, was poor in Brazil and he soon returned to Paris, his assistant Dr. Adolpho Lutz succeeding him as director of the institute. Lutz, the author says, conceived the idea long before Finlay that the mosquito was the possible transmitter of yellow fever. Much research has been done at this institute on bubonic plague, cholera, smallpox, dysentery and diphtheria.

The Butantan Institute was founded after the appearance of bubonic plague in 1899 in Santos primarily to prepare antiplague serum. Dr. Vital Brazil, the director, at the time of his appointment was himself recovering from plague. The Santos epidemic was the first outbreak of plague in Brazil. When plague disappeared the institute started a campaign to educate the public on the danger of venomous snakes and to develop a more effective treatment for snake bites. The interest thus created among the farmers is shown by the fact that they sent to the institute in its first five years of existence only 985 snakes and in the period from 1925 to 1936 a total of 50,000. This institute has become a world center for the study of venom and the preparation of serum to combat its effects.

Oswaldo Cruz, who had been in charge of the technical work in the manufacture of antiplague serum at the Butantan Institute, was made director of a new institute of experimental medicine, which within a few years was to be named in his honor. The Oswaldo Cruz Institute has various branches, each under a group of experts; among them are the branches of protozoology, helminthology, hematology, entomology and chemotherapy. The institute manufactures therapeutic products and maintains a hospital of tropical diseases, a museum of pathology and a library of 70,000 volumes. Dr. Cruz, on account of his campaigns to improve sanitation and to combat epidemics, was a prominent figure in South American medicine; at his death in 1917 Carlos Chagas became director of the institute, holding that position until his death in 1934. The chapter on the activities of the national health department emphasizes the campaign against leprosy. There are nearly 25,000 beds available or proposed for the care of lepers in Brazil. Yellow fever, although present in Brazil as early as 1686, was absent from Rio de Janeiro for many years after Oswaldo Cruz's campaign of sanitation. The federal government then decided to clean northeastern Brazil of yellow fever. The effort was unsuccessful and in 1923 the Rockefeller Foundation began its collaboration. The results at first were promising, but the disease was not completely eradicated and an unexpected outbreak occurred in Rio de Janeiro in 1928. Yellow fever was then found to be much more widespread in Brazil than had been previously recognized. It has been shown to be present in the jungles over enormous areas. The various yellow fever services in the country have been unified under one administration, and a satisfactory method of mass vaccination against yellow fever has been advanced.

Diseases of the Nose and Throat. By Charles J. Imperatori, M.D., F.A.C.S., Professor of Otolaryngology, New York Polyclinic Medical School and Hospital, New York, and Herman J. Burman, M.D., F.A.C.S., Adjunct Professor of Otolaryngology, New York Polyclinic Medical School and Hospital, New York. Second edition. Cloth. Price, $7. Pp. 726, with 480 illustrations. Philadelphia, Montreal & London: L. B. Lippincott Company, 1939.

Although the first edition of this book appeared in 1935, extensive additions and changes already have become necessary. Discussions of dermoid cysts of the nose, nasal telangiectasia, injuries to the nose, the cytology of nasal secretions, granulocytopenia, burning tongue, tuberculosis of the larynx, and other subjects have been added or extensively modified. The material has been presented in simple form with emphasis on symptoms, diagnosis and treatment. Some loose statements have crept in, such as "estimation of the severity of the luetic infection of the nose and throat can also be made from the intensity of the reaction" (Wassermann test). While not a conventional textbook or reference book, this should be found helpful to those who accompany their reading of the book with practical clinical and surgical experience.

Recollections of Student Life and Later Days. By C. J. Bond, C.M.G., F.R.C.S., F.L.S. A Tribute to the Memory of the late Sir Victor Horsley, F.R.S. Paper. Price, 1s. Pp. 47. London: H. K. Lewis & Co., Ltd., 1939.

The author was closely associated with Sir Victor Horsley in student life and later days. They roomed together for a time and traveled through Italy together. They helped each other in research work, each apparently inspiring the other. Horsley once asked Bond to state in writing his "own conception, not any one else's, of the nature of the soul." During a period of ill health, Horsley sent Bond a letter enclosing a beautifully made trephine about 4 mm. in diameter, suitable for trephining the skull of a frog. On his next vacation Bond, with the help of this instrument, removed both cerebral lobes from a toad. The animal recovered and could still catch worms and flies, but he had lost the instinctive habit of digging himself into loose ground at the approach of winter. The normal toad does this by an outward shoveling movement of the flexed hind legs, by which it lowers itself, tail end first, into the loose ground. Horsley, while surgical registrar at University College Hospital, spent several week ends with Bond at the Bedford Infirmary, and together they worked on a study of the salivary glands in woodpeckers. Once, after working in the wards all day, Horsley suggested to Bond that they spend the night in operating on a corpse in the postmortem room. This was done and they resumed work in the wards the following day. This particular surgical experience, Bond says, was useful as he was approaching the final F.R.C.S. examination. They arranged their sojourn in Italy so that travel from one place to another would be at night in order to save hotel expenses. The author relates experiences in their long association which have not been referred to previously except perhaps incidentally.

The Anaerobic Bacteria and Their Activities in Nature and Disease: A Subject Bibliography. By Elizabeth McCoy, Department of Agricultural Bacteriology, University of Wisconsin, Madison, and L. S. McClung, George Williams Hooper Foundation for Medical Research, University of California, San Francisco. Volume I: Chronological Author Index. Volume II: Subject Index. Cloth. Pp. 295; 602. Berkeley: University of California Press, 1939.

This is a bibliography of literature concerning the anaerobic bacteria. The authors have examined, in the original with few exceptions, 10,500 journal articles and other published reports. While they do not claim that this is a complete index of all published articles in the field, reference to any important article not included may be obtained from the bibliographies of the the articles listed. The first volume is a chronological author index beginning with the year 1816. The second volume is a subject index, the names of authors appearing under each subject in alphabetical order. The subjects in the second volume under which the literature is classified include (1) habitat, with subsections referring to dairy products, soil, mud, sand, street dust, water, the intestinal tract of man and of animals, internal organs, urogenital system, circulatory system, the eyes, the skin, the muscles, the bone marrow, foods, surgical materials, ammunition and the air; (2) culture methods, with subsections designated as mediums for counting, mediums for spore production, synthetic mediums, single cell isolation methods, dye stasis, physical methods of culture, chemical methods of culture and stock culture mediums; (3) morphology, and (4) metabolism, including fermentation of sugars and other products, nitrogen fixation and the products of metabolism, e. g. ethyl, butyl, amyl and isopropyl alcohols, acetone and pigments. Succeeding classifications include the subjects of physiology, serology and disease relations (botulism, tetanus, gangrene, prophylactic and therapeutic use of antitoxin). A large section on classification has numerous subsections. These volumes illustrate the enormous amount of labor involved in preparing a more or less complete bibliography on any medical subject. The material represents about five years of research and reading, during which time, however, only a few months was available to one of the authors for full time work.

Il trattamento delle sindromi parkinsoniane postencefalitiche con le radici di Atropa belladonna. Dal Prof. Dott. Fedele Negro, direttore della Divisione neuropatologica dell'Ospedale S. Giuseppe Cottolengo in Torino. II. Collana monografica di "Schizofrenie." Paper. Price, 15 lire. Pp. 79, with 3 illustrations. Turin: Industrie Tipografico-Editoriali Riunite, 1938.

This is a monograph on the treatment of the postencephalitic parkinsonian syndrome with the root of atropine (belladonna). The first and second chapters deal with true Parkinson's disease and the parkinsonian syndrome of postencephalitis, the third with the therapy of the postencephalitic parkinsonian syndrome, and the fourth and fifth with the need of treatment and the progressive nature of this affliction. The author believes that hospital management is essential in the first few months of treatment. A detailed plan is given regarding the preparation of the belladonna root. Both Bulgarian and Italian belladonna roots were used. There is a complete bibliography on this form of treatment and, interestingly, all the contributors are from Italy. This monograph is recommended to all neurologists.

You Can't Eat That! A Manual and Recipe Book for Those Who Suffer Either Acutely or Mildly (and Perhaps Unconsciously) from Food Allergy. By Helen Morgan. Foreword by Dr. Walter C. Alvarez. Cloth. Price, $2.50. Pp. 330. New York: Harcourt, Brace & Company, 1939.

This is another book on food allergy, written especially for the public. In the four short chapters in part I, the author endeavors to answer the questions "What is allergy?" and "What causes allergy?" and to show how allergic conditions are diagnosed and treated. One of the most interesting parts of the book is the preface, by Walter C. Alvarez, in which he shows how to work out problems in food allergy by the use of elimination diets. The chapter on hints in general cookery is a preface to numerous chapters containing recipes and instructions on how to prepare salads, vegetables, sauces, meats, desserts, breads, cakes and relishes. Part III opens with a chapter entitled "What's In It?" in which popular food products are listed and their actual content given. There are lists also, for example, of the kinds of crackers which contain no eggs, of sweet cakes which contain no eggs and of cereals, cakes and crackers which contain no milk. There is a short chapter on "Jokers in Cooked Foods," to show the allergic person what he may eat unexpectedly when he dines out, for chefs have numerous tricks of throwing in a little of this or that to improve the taste of food. Source foods are listed to show into what products they are made. Wheat, corn, rye, rice, oats, buckwheat, orris root, cottonseed and olives, for example, appear in some of the most unexpected dietary concoctions. The final chapter is an index to enable the reader to find quickly the foods listed in this book which are made without any of the common allergens.

The Newer Knowledge of Nutrition. By E. V. McCollum, Ph.D., Sc.D., LL.D., Professor of Biochemistry, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, Elsa Orent-Keiles, Sc.D., Associate in Biochemistry, School of Hygiene and Public Health, The Johns Hopkins University, and Harry G. Day, Sc.D., Associate in Biochemistry, School of Hygiene and Public Health, The Johns Hopkins University. Fifth edition. Cloth. Price, $4.50. Pp. 701. New York: Macmillan Company, 1939.

The authors have concisely surveyed the field of nutrition. The present edition has been completely rewritten but the plan of the book is essentially the same. The first two chapters are historical, tracing the development of the modern concepts in nutrition. Then follow chapters on carbohydrates, lipids, proteins, amino acids, calcium, phosphorus and magnesium, sodium, potassium, chlorine, iron, copper and the nutritional anemias. The latter half of the book is largely devoted to discussions of the vitamins. Following full discussions of the better known vitamins is a chapter on other vitamin factors in which appear such terms as factor Y, factor W, factor U, the anti-gizzard erosion factor, the grass juice factor, the chick antiencephalomalacia factor and lactation factors. These terms, which have not yet percolated strongly into the general literature, indicate that the vitamin factors are more numerous than was suspected and that other discoveries in this field are to be expected. Following the chapters on vitamins are discussions of the dietary properties of foodstuffs, the dietary habits of man and diet in relation to teeth and longevity and several appendixes giving the comparative nutritive value of numerous foods and the distribution of vitamins in foods. Preceding the index are pictures of different organs to show the effect on them of specific food deficiencies.

Bergey's Manual of Determinative Bacteriology: A Key for the Identification of Organisms of the Class Schizomycetes. By David H. Bergey, Robert S. Breed, E. G. D. Murray and A. Parker Hitchens. Assisted by R. E. Buchanan et al. Fifth edition. Cloth. Price, $10. Pp. 1,032. Baltimore: Williams & Wilkins Company, 1939.

There have been numerous attempts to arrange the species of bacteria in natural systems of classification. The first simple system of Müller listed but two genera (Vibrio and Monas), which included organisms that would today probably be accepted as bacteria. The present manual was first published sixteen years ago. The first edition contained tabulated descriptions of 832 species of bacteria, while the present edition contains descriptions of 1,335 species with a reference to the original place of publication of 5,600 descriptions. The increase in number is due chiefly to the recognition of groups of genera which seem to be related to one another yet distinct from other groups. Nine new generic names are used: Noguchia, Microbacterium, Fusobacterium, Pasteuria, Caulobacter, Proactinomyces, Malleomyces, Veillonella and Blastocaulis. In spite of the extensive rearrangement of genera and the use of nine new generic terms, few new binominals have been formed and no trinominals are used. It is difficult to prepare a satisfactory outline of classification of bacterial genera and species, especially because the material is in itself incomplete. The authors hope that the classification used in this book will be employed generally. They request the cooperation of all interested persons in the further development of this field of bacteriology. Suggestions for using this manual are followed by an interesting and extensive historical survey of classifications of bacteria with emphasis on the ones proposed since 1923. They review the international rules of nomenclature and discuss how bacteria are named and identified. In the main body of the book under the various family names they give in tabulated form the origin of the name of the species, the reference to the first description, and many details regarding morphology, cultural characteristics, source, habitat and diseases, if any, which they may produce.

Studies on Drug Addiction, with Special Reference to Chemical Structure of Opium Derivatives and Allied Synthetic Substances and Their Physiological Action. By Lyndon F. Small, Consultant in Alkaloid Chemistry, U. S. Public Health Service, University of Virginia, Charlottesville, Nathan B. Eddy, Consultant Biologist in Alkaloids, U. S. Public Health Service, University of Michigan, Erich Mosettig, Research Associate in Organic Chemistry, University of Virginia, and C. K. Himmelsbach, Passed Assistant Surgeon, U. S. Public Health Service. Prepared by direction of the Surgeon General. U. S. Treasury Department, Public Health Service. Supplement No. 138 to the Public Health Reports. Cloth. Price, 60 cents. Pp. 143. Washington, D. C.: Supt. of Doc., Government Printing Office, 1938.

The volume presents various studies conducted by the Division of Medical Sciences of the National Research Council. The chemical and pharmacologic studies were done at the Universities of Virginia and Michigan, respectively. The book is divided into three parts. The first section is devoted to some relationships between chemical constitution and pharmacologic action in the morphine series; the second outlines various attempts made to synthesize substances with narcotic and, in particular, analgesic action, and the third reviews clinical studies of drug addiction, with special reference to opium and allied synthetic substances. This is a notable compilation and should prove an aid to persons interested in chemical and pharmacologic investigations.

Die endokrinen Drüsen des Gehirns: Epyphyse und Hypophyse. Ein Blick in ein interessantes Gebiet. Von Dr. med. Paul Niehans, Chirurg F. M. H. der Klinik von Clarens und der Spitäler von Vevey und Montreux (Schweiz). Cloth. Pp. 280. Berne: Medizinischer Verlag Hans Huber, 1938.

This is a review of the laboratory and clinical knowledge concerning the epiphysis and hypophysis, mainly the latter. Twenty-five separate pituitary hormones are accepted and discussed by the author. For each hormone the history, origin, function, deficiency and excess manifestations, clinical conditions in which it is involved and medical and surgical treatment are outlined. Unfortunately the author fails to sift or evaluate the literature reviewed, so that in consequence the book is a collection of fact and fiction which has accumulated for the past hundred years. Many general conclusions and dogmatic statements are made concerning problems and observations which are still unsubstantiated. Much significant laboratory and clinical work concerning the hypophysis is not mentioned. Treating endocrine deficiencies by transplanting animal glands is the recurrent theme. The author's own work in transplantation figures largely in the book, although this method has not had recognition in the literature. There is no bibliography.

The Vaginal Diaphragm: Its Fitting and Use in Contraceptive Technique. By Le Mon Clark, M.S., M.D. Cloth. Price, $2. Pp. 107, with 53 illustrations. St. Louis: C. V. Mosby Company, 1939.

This brief monograph relates solely to the diaphragm and jelly combination method of contraception, which is extensively used today. The method is fully described and well illustrated, so that the physician who wishes to acquaint himself with the details of the procedure will find the work entirely adequate. There is no attempt on the part of the author to discuss the various methods of birth control or to compare their relative merits. He limits his discussion to the vaginal diaphragm used in combination with a spermicidal jelly and recommends this method to patients who desire such protection.

Orthopedic Appliances: The Principles and Practice of Brace Construction for the Use of Orthopedic Surgeons and Bracemakers. By Henry H. Jordan, M.D. Foreword by E. G. Brackett, M.D. Cloth. Price, $4. Pp. 412, with 176 illustrations. New York, Toronto & London: Oxford University Press, 1939.

There is no question that this book is timely. There has been an urgent need for a guide to the technic and manufacture of braces as well as to the plaster of paris technic which is necessary in their construction. The author has covered a vast ground and has covered it creditably. However, the most valuable part of the book is the chapter dealing with the plaster of paris and the brace model technic. The principle of construction is particularly well brought out in the description of body corsets, which goes into minute details. What one misses in the book is descriptions of many practical, excellent orthopedic devices used in this country, for instance Funsten's pronation splint for pronation contracture and the spring back brace. On the other hand, the description of the different hinges and particularly the different types of knee joint locks, with mechanical construction drawings, is very valuable. Splints for the upper extremity are fairly well represented, e. g. abduction, cock-up and different types of finger splints. There is a chapter on the use of x-rays for landmarking and checking up on the construction of braces. On the whole, this is a valuable book, even though it does not quite do justice to the development of the brace technic in this country. It is the only book in the English language that has so far appeared on this subject and is indispensable to the orthopedic surgeon.

Der Rheumatismus: Sammlung von Einzeldarstellungen aus dem Gesamtgebiet der Rheumaerkrankungen. Herausgegeben von Professor Dr. Rudolf Jürgens, Stellv. Direktor der Universitätsklinik für natürliche Heil- und Lebensweisen und Chefarzt des Augusta-Hospitals Berlin. Band XIV: Chirurgie und rheumatische Krankheiten. Von Dozent Dr. A. Fonio, Chefarzt des Bezirksspitals Langnau (Bern, Schweiz). Band XV: Der Muskelrheumatismus. Von Professor Dr. Max Lange, Krankenhaus Rotes Kreuz, München. Boards. Price, 15 marks; 6 marks. Pp. 235, with 26 illustrations; 84, with 20 illustrations. Dresden & Leipzig: Theodor Steinkopff, 1939.

This contribution to the series of monographs on rheumatism consists principally of a brief description of the various diseases which may affect the joints or which may produce symptoms referable to the joints. Although surgery appears in the title, the only surgical bias seems to be in the citation of a considerable number of articles from surgical journals. One wishing to consult this monograph for suggestions on the surgical treatment of various disorders of the joints would be disappointed.

Prof. Max Lange classifies muscular rheumatism as infectious and noninfectious. After brief discussions of the clinical aspects, he considers the diagnosis and differential diagnosis. The treatment is given in considerable detail and includes, with much excellent advice, some discussions which cannot be considered as representing a scientific approach. The bibliography contains not a single reference outside the German literature.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Osteopathy: "As Taught and Practiced in the Legally Incorporated Colleges of Osteopathy of Good Repute" Construed.—In 1901 the medical practice act of Kansas was amended to authorize the board of medical registration and examination to license persons to practice osteopathy. The amendment specifically prohibited persons so licensed from administering drugs or medicines of any kind and from performing operations in surgery. In 1913 an osteopathic practice act was enacted creating a state board of osteopathic examination and registration, prescribing qualifications to be possessed by applicants for licenses and authorizing the board to issue to a successful applicant "a certificate granting him the right to practice osteopathy in the state of Kansas, as taught and practiced in the legally incorporated colleges of osteopathy of good repute." The defendant, Gleason, obtained a license to practice osteopathy under the act of 1913 and owned and operated a hospital at Larned, Kan. The state, on the relation of the Attorney General, instituted quo warranto proceedings in the Supreme Court of Kansas against Gleason, contending that he was engaged unlawfully in the practice of medicine and surgery and asking the court, in effect, to enjoin him from so practicing.

The petition, among other things, alleged that Gleason, not having a license issued by the board of medical registration and examination, administered medical and surgical treatment to numerous patients in his hospital and that he permitted other osteopaths to render similar treatment in the hospital. Gleason admitted that he had no license issued by the board of medical registration and examination, that he was licensed to practice osteopathy and that he had for many years treated patients both medically and surgically. He contended that his license to practice osteopathy authorized him to engage in the practice of medicine and surgery, including drug therapy, because the

school from which he graduated in 1915, the American School of Osteopathy of Kirksville, Mo., taught then and in 1913 when the osteopathic act was enacted the use of medicine and surgery, including drug therapy, for the treatment and alleviation of human ills. He contended that the osteopathic school or system of healing includes the practice of medicine and surgery and that colleges of osteopathy use the same textbooks on the practice of medicine and surgery as are used in approved schools of medicine generally and devote sufficient time to these subjects to qualify graduates in the use and practice of medicine and surgery. He admitted permitting other osteopaths to practice medicine and surgery in his hospital.

Since the enactment of the osteopathic act in 1913, the Supreme Court said, Kansas has had two boards of examiners, composed of persons having different educational qualifications, issuing different types of certificates. One, the board of medical registration and examination, is composed of members who have received the degree of doctor of medicine from some reputable medical college or university. It is authorized to issue certificates "to practice medicine and surgery." The other, the board of osteopathic registration and examination, is composed of osteopaths, graduates of a reputable school or college of osteopathy. It is authorized to issue certificates "to practice osteopathy." By these separate acts, the court thought, the legislature clearly recognized a distinct difference between the practice of medicine and surgery and the practice of osteopathy. The court pointed out that a certificate authorizing one to practice osteopathy, whether issued prior to 1913 by the board of medical registration and examination or since that time by the board of osteopathic registration and examination never has been recognized by the laws of Kansas, nor by the courts of Kansas, as authorizing its holder to engage in the practice of medicine and surgery. Osteopaths in Kansas are limited to the practice of osteopathy in harmony with the fundamental principles of osteopathy as generally known and understood and as taught in osteopathic schools or colleges of good repute in 1901 and 1913. While osteopaths, the court continued, are expected to continue to study, to make progress, to learn more about their profession and to apply such knowledge in their practice, yet they are still limited to the practice of osteopathy as that science or system was known and understood when the laws under which they were licensed were enacted. If, as suggested by Gleason, osteopathy has abandoned its fundamental opposition to drug therapy and operative surgery, meaning by that term surgery by the use of surgical instruments, and now includes the use of those things in its system of healing, that fact, the court said, never has been recognized by the legislature of Kansas.

The defendant argued that since the osteopathic act required an applicant to be examined in surgery a licentiate was authorized to practice surgery generally, including operative surgery. But, said the court, the word "surgery" as used in the osteopathic act means surgery by manual manipulation. The general use of a knife or other instruments in surgical operations was regarded as unnecessary and opposed to the osteopathic system of treatment. Gleason further pointed out that the prohibition contained in the law of 1901 denying to osteopaths the right to administer drugs or medicine of any kind and the right to perform operations in surgery was omitted in the 1913 act and contended that this omission constituted an authorization for licentiates under the 1913 act to engage in such practice. It seemed clear to the court that the legislature intentionally omitted the prohibition from the 1913 act but that it did not follow that thereby the legislature intended to confer unrestricted authority on osteopaths to administer drugs and perform operations in surgery. Considering the fact that surgery in its primitive and broadest sense, the court said, includes adjustment of bones, muscles, ligaments and nerves by manual operation, and that skill in doing so is taught in osteopathic schools and colleges and occupies a major place in the science or system of osteopathy, the prohibition against osteopaths performing operations in surgery contained in the 1901 act was an inaccurately used expression and should have been omitted from the 1913 act for that reason alone. Furthermore, the system of osteopathy, generally speaking, strongly opposed the use of drugs as remedial agencies in the treatment of the sick, afflicted or injured. Osteopathic schools and colleges of good repute contained no course for the study of materia medica. There was no real occasion, therefore, to prohibit osteopaths from using drugs, since they made no claim or pretense of doing so, nor did they study to qualify themselves for such use. The legislative intent of the act of 1913 was, the court repeated, to recognize the system of osteopathy as then taught in its schools and colleges of good repute. What was then taught in osteopathic schools was a matter of common knowledge. Their courses of study were available, as were the writings of its founder and other leading osteopathic teachers and practitioners. Osteopathy could be as readily designated by the language used in the act as in any other way. The act was not void for uncertainty in its failure more specifically to define osteopathy nor was it, as construed by the court, void as unconstitutional because it delegated to legally incorporated colleges of osteopathy the right to determine the methods and scope of practice of osteopathy in Kansas. The act, however, did not authorize the state board of osteopathic registration and examination to approve schools or colleges which did not conform their teachings to the fundamental principles of osteopathy.

The medical practice act, in providing that its provisions shall not apply to any registered osteopathic physician, means no more than that one who desires to practice osteopathy is not required to make application to the state board of medical registration and examination and have that board pass on his qualifications and issue to him a certificate to practice osteopathy. It does not mean that none of the provisions of the medical practice act applies to osteopaths, and hence that osteopaths may practice medicine and surgery in all particulars with impunity. Any other construction, the court said, would render ludicrous and nugatory the work of the legislature in treating the practice of medicine and surgery as one thing and the practice of osteopathy as another.

The osteopathic act, the court concluded, did not authorize licentiates to use drugs, in so far as such drugs are given as remedial aids. It did not authorize them to practice in the general field of operative surgery with surgical instruments but limited them to manipulative surgery.

The court, therefore, ousted defendant Gleason from the practice of medicine and surgery. The court declined to oust him from permitting other licensed osteopaths to practice medicine and surgery generally in his hospital. Such an order would, the court pointed out, require the defendant to watch continuously what other licensed osteopaths did in his hospital, and this burden should not be put on the defendant.—*State ex rel. Beck, Atty. Gen. v. Gleason (Kan.), 79 P. (2d) 911; 83 P. (2d) 425.*

Society Proceedings

COMING MEETINGS

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 7-9. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.

American Association of Railway Surgeons, Chicago, Sept. 11-13. Dr. Daniel B. Moss, 547 West Jackson Blvd., Chicago, Secretary.

American Congress of Physical Therapy, New York, Sept. 5-8. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.

American Roentgen Ray Society, Chicago, Sept. 19-22. Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal, Can., Secretary.

Idaho State Medical Association, Boise, Aug. 23-26. Dr. J. N. Davis, 204 Fourth Avenue East, Twin Falls, Secretary.

Kentucky State Medical Association, Bowling Green, Sept. 11-14. Dr. Arthur T. McCormack, 620 South Third St., Louisville, Secretary.

Michigan State Medical Society, Grand Rapids, Sept. 18-22. Dr. L. Fernald Foster, 311 Center Ave., Bay City, Secretary.

National Medical Association, New York, Aug. 14-18. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.

Nevada State Medical Association, Reno, Sept. 22-23. Dr. Horace J. Brown, 120 North Virginia St., Reno, Secretary.

North Pacific Society of Internal Medicine, Vancouver, B. C., Sept. 1-2. Dr. Lester J. Palmer, 1115 Terry Ave., Seattle, Secretary.

Oregon State Medical Society, Gearhart, Sept. 6-9. Dr. M. L. Bridgeman, 1020 S.W. Taylor St., Portland, Secretary.

Rocky Mountain Medical Conference, Salt Lake City, Sept. 5-7. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver, Secretary.

Utah State Medical Association, Salt Lake City, Sept. 5-7. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.

Washington State Association, Spokane, Aug. 28-30. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary

Wisconsin, State Medical Society of, Milwaukee, Sept. 13-15. Mr. J. G. Crownhart, 119 East Washington Ave., Madison, Secretary.

Wyoming State Medical Society, Salt Lake City, Utah, Sept. 5-7. Dr. M. C. Keith, 156 South Center St., Casper, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1929 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

8: 421-492 (June) 1939

The Community Hospital. W. H. Anderson, Booneville, Miss.—p. 421.

Hospitalization of Alabama's Indigent Sick. A. C. Jackson, Jasper.—p. 424.

Hospital Service Corporation of Alabama. F. H. Craddock, Sylacauga.—p. 426.

Medical Care of Coffee County Farm Security Administration Clients. E. L. Gibson, Enterprise.—p. 428.

Wilcox County and Gees Bend Plans of Medical Care. J. P. Jones, Camden.—p. 430.

American Journal of Clinical Pathology, Baltimore

9: 257-380 (May) 1939

Critique of Chemical Procedures Used in Clinical Diagnosis. M. Bodansky, Galveston, Texas.—p. 257.

Subacute Bacterial Endocarditis Treated with Sulfanilamide Resulting in Granulocytopenia and Death. S. Sailer, New York.—p. 269.

Experimental Tissue Lesions with Mixtures of Human Fat, Fatty Acids, Soaps and Cholesterol. E. F. Hirsch, Chicago.—p. 279.

Pathologic Changes Produced by Chlorinated Lard. D. H. Drummond, M. F. Gunderson and J. P. Tollman, Omaha.—p. 286.

Infectious Mononucleosis. E. A. Marshall, Cleveland.—p. 298.

Wassermann Reaction in Infectious Mononucleosis. W. Saphir, Chicago.—p. 306.

Relation of Trauma to Leukemia. A. Yaguda, Newark, N. J., and N. Rosenthal, New York.—p. 311.

Problem in Blood Grouping. E. M. Katzin and P. Levine, New York.—p. 316.

Simplified Method for Preparation of Antigen for Use in Complement Fixation Test for Syphilis. F. Boerner, C. A. Jones and Marguerite Lukens, Philadelphia.—p. 321.

*Basophilic Aggregations in Blood of the Newly Born: (A) Laboratory Animals; (B) Humans. C. P. McCord and W. R. Bradley, Detroit.—p. 329.

Diagnosis of Tuberculosis in Ten to Twelve Days by Guinea Pig Inoculation. F. L. Pickof, Los Angeles.—p. 339.

Endometriosis. T. C. Moss, Memphis, Tenn.—p. 345.

Foreign Body in Hepatic Ducts Producing Obstructive Jaundice of Seven Years' Duration with Internal Biliary Fistula. B. L. Crawford and H. L. Stewart, Philadelphia.—p. 353.

Primary Carcinoma of Liver in a Child: Case Report. D. H. Drummond and J. P. Tollman, Omaha.—p. 361.

Basophilic Aggregations in the Newborn.—Since it is known that the blood of the fetus and the newborn of many animals contains immature cell forms, McCord and Bradley tried to establish percentages of basophilic aggregations at short intervals after birth in order to fix the time at which substantially constant numbers of basophilic aggregations begin to exist. They found that, as in the case of laboratory animals, newborn infants present basophilic aggregations obtained from circulating blood in numbers and percentages in excess of adult, healthy individuals. The maximal basophilic aggregation percentage, which averages 5.3, was present during the first twenty-four hours after birth both in premature and in full term infants. Unlike animals, a diminution to adult percentages took place rapidly, and usually at about the eighth day a normal level was reached. Continuation of testing in premature infants to the end of forty days after birth indicates no substantial rise after normal percentages have been reached. Occasion for the application of the basophilic aggregation test in instances of suspected lead poisoning in young children is not nullified on the assumption that children more than 10 days old may continue to exhibit high percentages of these cells. In young albino rats, high percentages of erythrocytes containing basophilic substance persist until near the hundredth day of life. This fact militates against their use in certain experimental studies, particularly with lead.

American Journal of Pathology, Boston

15: 279-390 (May) 1939

Antigenicity of Virus of Trachoma. L. A. Julianelle, St. Louis.—p. 279.

Reaction to Killed Tubercle Bacilli in Normal and Immunized (Sensitized) Rabbits. C. T. Olcott, New York.—p. 287.

Skin Tumors Following Single Application of Methylcholanthrene in C57 Brown Mice. G. B. Mider and J. J. Morton, Rochester, N. Y.—p. 299.

Studies on Pathogenicity and Cytologic Reactions of Submaxillary Gland Virus of the Guinea Pig. C. T. Rosenbusch and A. M. Lucas.—p. 303.

Histology of Orbital and Other Fat Tissue Deposits in Animals with Experimentally Produced Exophthalmos. G. K. Smelser, New York.—p. 341.

*Cerebral Vascular Disease Accompanying Sickle Cell Anemia. W. H. Bridgers, Durham, N. C.—p. 353.

Pathologic Changes Following Therapeutic Hyperthermia: Report of Case. L. Lichtenstein, New York.—p. 363.

Lymphoid Nodules of Human Bone Marrow. R. J. Williams, Providence, R. I.—p. 377.

Studies on Rapidly Developing Intestinal Adenoma in a Pig. H. E. Biester, L. H. Schwarte and D. F. Eveleth, Ames, Iowa.—p. 385.

Cerebral Vascular Disease and Sickle Cell Anemia.—A clinical and pathologic study of two cases of sickle cell anemia accompanied by symptoms of cerebral vascular disease is reported by Bridgers because of its contribution to the pathogenesis of the disorders of the central nervous system in sickle cell anemia. The two cases show that sickle cell anemia may first become manifest through the appearance of signs and symptoms indicative of cerebral vascular disease. The clinical features in such cases lead to the diagnosis of either cerebral vascular thrombosis or intracranial hemorrhages. The pathologic changes seen in one of the cases establish the fact that in sickle cell anemia the large subarachnoid cerebral arteries may undergo gradual obliteration with final complete closure through the operation of a process identical with that which results in occlusion of the splenic arteries. This process is one of endarterial intimal proliferation and not of thrombosis. In the second case the necropsy showed that another vascular process, quite different from endarterial intimal proliferation, also occurs in sickle cell anemia. This process develops in connection with the small intracerebral vessels and may result in multiple focal necroses and hemorrhages in the brain, in contrast with the large infarcts that characterize the proliferative obstructive process in the larger arteries. The nature of this second process is not clear.

American Journal of Public Health, New York

29: 427-582 (May) 1939. Partial Index

Malnutrition: A Challenge and an Opportunity. F. G. Boudreau and H. D. Kruse, New York.—p. 427.

*Comparison of Indexes Used in Judging Physical Fitness of School Children. Susan P. Souther, Hartford, Conn.; Martha M. Eliot and Rachel M. Jenss, Washington, D. C.—p. 434.

Sanitary Condition of Paper Containers for Retail Packaging of Perishable Foods. J. R. Sanborn, Geneva, N. Y.—p. 439.

*Specific and Nonspecific Serum Treatment of Scarlet Fever. F. H. Top and D. C. Young, Detroit.—p. 443.

Social Security Needs for Vital Statistics Records. W. C. Smith and I. S. Falk, Washington, D. C.—p. 452.

Preparation of the Nurse of the Future. Leah M. Blaisdell, New York.—p. 467.

Interpreting the Physician and Making Him a Part of the Health Education Program. Mary P. Connolly, Detroit.—p. 473.

New Appraisal Form for Local Health Work. W. F. Walker, New York.—p. 490.

Practical Methods for Control of Hygienic Exposures. G. A. Coburn, Anderson, Ind.—p. 501.

Physical Fitness of School Children.—Souther and her associates limit their study to the ability of each of four indexes of body build to identify children who are likely to be physically unfit, using as criteria of reference the observations of the physician with respect to the child's general nutritional condition and the child's annual rate of gain in weight. The indexes studied were the Baldwin-Wood height-weight index, the Pryor width-weight index, the nutritional status indexes of Franzen and his co-workers and the arm-chest-hip index. Each index has been set to identify, for the purpose of this study, the lowest 15 per cent of the boys and girls. The 713 boys and girls 7 years of age selected have been defined arbitrarily as the group most likely to be in need of medical care or nutritional assistance. A single pediatrician made two

annual physical examinations of each child. At the same time a single technician took the necessary anthropometric measurements according to the prescribed technics. The children's medical history and their socio-economic status were ascertained, and they were weighed at quarterly intervals during the period of observation (from nineteen to twenty months). The agreement between the physician's clinical judgment and each of the indexes is that the physician who examined these children classified forty of the 348 girls as poorly nourished at 7 years of age. The Baldwin-Wood index identified twenty-five girls, or 63 per cent of these forty, as underweight. When the Pryor width-weight index was applied only 28 per cent of the forty girls were picked out as underweight, and with the arm-chest-hip index the percentage identified as below par was somewhat less (10 per cent). The results of testing the nutritional status indexes show that the weight index identified only 3 per cent, and the indexes for arm girth and subcutaneous tissue picked out 5 per cent of the forty girls. Assuming that the children who exhibited an unsatisfactory percentage gain in weight (those in the lowest 10 per cent of the group) were likely to be in a poor physical condition, the results of the comparison between annual percentage gain in weight, so far as showing the usefulness of any of the four indexes, are even more discouraging. The Baldwin-Wood index showed the maximal agreement (29 per cent), while the nutritional status index for weight failed to identify any of the thirty-five girls whose weight gain was considered unsatisfactory. Similar analyses of the boys indicate that the indexes also failed to identify a large number of the boys whom the physician judged to be poorly nourished or whose weight gain was markedly below average. Since such indexes do not furnish the school health officer with a satisfactory method of identifying a child who may be in need of medical attention or nutritional assistance, the clinical examination must certainly form an integral part of the assessment, especially if determining the need of medical care is to be one of the objectives of a school health program. Until the physician is furnished with more satisfactory and practical tools for evaluating the child's physical fitness, it may be wise to supplement the clinical examination with some simple measure of the child's progress, such as his relative gain in weight. Observations made on the 713 children are being used to investigate this problem.

Serum Treatment of Scarlet Fever.—Top and Young studied the therapeutic effect of scarlet fever convalescent serum, scarlet fever antitoxin and a nonspecific serum during a period of one year. During this time, 995 patients with moderately severe scarlet fever were admitted to the hospital and received a single dose of one of the serums by the intramuscular route. The study was controlled by alternating the administration of the serums. No statistical difference was demonstrated between the serum groups when certain status on admission factors were tested. Convalescent serum and antitoxin exerted a similar therapeutic effect. The value a scarlatinal serum exhibits in the treatment of moderately severe scarlet fever does not appear to be gaged entirely by its antitoxin content. There was about one sixth the value in using nonspecific serum in the treatment of moderately severe scarlet fever as there was in using specific serum.

American Journal of Tropical Medicine, Baltimore

19: 207-308 (May) 1939

Beriberi and B_1 Hypovitaminosis. G. C. Shattuck, Boston.—p. 207.
Possible Clinical Significance of Factors of the Vitamin B_2 Complex Other Than Nicotinic Acid. W. J. Dann, Durham, N. C.—p. 219.
Newer Clinical Aspects of Vitamin Deficiency Diseases: Vitamin A Deficiency. J. B. Youmans, Nashville, Tenn.—p. 229.
Nontropical Sprue: Case Report. A. C. Reed, San Francisco.—p. 243.
Evaluation of the Role of the Food Handler in Transmission of Amebiasis. J. J. Sapero and C. M. Johnson, Panama, Republic of Panama.—p. 255.
Preliminary Note on Identity, Life Cycle and Pathogenicity of an Important Nematode Parasite of Captive Monkeys. A. O. Foster and C. M. Johnson, Panama, Republic of Panama.—p. 265.
Exo-Erythrocytic Stages in Asexual Cycle of Plasmodium Circumflexum. R. D. Manwell and F. Goldstein, Syracuse, N. Y.—p. 279.
Effect of Various Diluents Acting for Short Periods on Rabies Virus in High Dilutions. D. F. Milam, Montgomery, Ala.—p. 297.

Archives of Dermatology and Syphilology, Chicago

39: 955-1104 (June) 1939

Occupational Melanosis from Pitch. H. R. Foerster, Milwaukee, and L. Schwartz, Washington, D. C.—p. 955.
*Acetarsone Therapy in 187 Cases of Congenital Syphilis, with Observations on Group of Eighty-Seven Patients Receiving No Treatment. D. M. Pillsbury and H. H. Perlman, Philadelphia.—p. 969.
Blood Urticaria, Including Contribution on Metallergic Genesis of Cold Urticaria. E. Urbach, Philadelphia; F. Linneweh, Berlin, Germany, and S. Greenberg, New York.—p. 987.
Chronic Relapsing Urticaria and Angioneurotic Edema: Report of Case with Associated Pancreatic Insufficiency and Relief by Oral Administration of Deinsulinized Pancreatic Extract. J. Markel, Manchester, Pa.—p. 992.
*Cryotherapy for Acne and Its Scars. F. L. Karp, H. A. Nieman and C. Lerner, New York.—p. 995.
Syphilitic Reagin in Blood and in Spinal Fluid: Comparative Quantitative Study. A. S. Wiener and I. M. Derby, Brooklyn.—p. 999.
Pathologic Fracture Due to Syphilis: Report of Case with Bizarre Roentgen Findings and Favorable Response to Therapy. A. L. Weiner, Cincinnati.—p. 1006.
Lichenificatio Gigantea (Lichénification Géante of Brocq and Pautrier). C. Berlin, Tel Aviv, Palestine.—p. 1012.
Scleroderma Associated with Adrenal Neoplasm: Report of Case. G. B. Barlow, Englewood, N. J.—p. 1021.
Hereditary Multiple Telangiectasia (Rendu-Osler Disease). V. Pardo-Castello and E. Pastor Fariñas, Habana, Cuba.—p. 1025.
Kaposi's Varicelliform Eruption: Report of Five Cases, in One of Which the Condition Began as Herpes Zoster. A. D. King, Wilmington, Del.—p. 1035.
Sheep Pox Infection in Man. A. Schoch, Dallas, Texas.—p. 1040.

Acetarsone for Congenital Syphilis.—Pillsbury and Perlman have followed 187 children with congenital syphilis who were given acetarsone for periods varying from two months to six and one-half years. In eighty-seven of these cases the average period between registration of the patient and the diagnosis of syphilis was three years. The effect of acetarsone alone in reversing the Wassermann and the Kahn reaction of the blood has been only moderately satisfactory for infants less than 6 months of age but as good as that of standard preparations, or better, for older children. The incidence of all reactions has been 10.7 per cent; that of serious reactions, particularly nephritis, 4.6 per cent. For newborn infants the use of a system (Bratusch-Marrain) of dosage based on weight is essential; reactions are reduced but not entirely prevented by this means. Nephritic reactions occurring suddenly and insidiously are the greatest single drawback to acetarsone therapy. The authors do not believe that administration of the drug should be resumed after such a reaction. In general, the occurrence of gastrointestinal and dermatitic reactions does not contraindicate further acetarsone therapy. Acetarsone is probably not administered as directed to patients treated at home, as the incidence of reactions among patients treated under controlled hospital conditions was four times that observed among outpatients. Among the eighty-seven children observed for more than three years after acetarsone therapy, one serologic relapse occurred. No instance of clinical relapse of a lesion not present when treatment was started has been observed. There were twenty-two clinical relapses among the eighty-seven children who were under medical observation for an average of three years before antisyphilitic treatment was given. The responsibility of the parent or guardian is one of the most important features of treating congenital syphilis with acetarsone by mouth, and lack of cooperation by the parent is a sufficient contraindication to acetarsone therapy. The effect of acetarsone in arresting congenital syphilis is inferior to that of arsphenamine and bismuth preparations. The performance of a routine Wassermann test of the blood and of a precipitation test are absolutely essential to an adequate pediatric examination.

Cryotherapy for Acne and Its Scars.—Karp and his associates treated fifty cases of acne or postacne scars with a mixture of solid carbon dioxide, acetone and precipitated sulfur. The acetone serves a triple function: it dissolves the sebum, it seems to increase the speed with which the solid carbon dioxide changes to the gaseous state with consequent further lowering of the temperature and it produces a more uniform paste. Applications are repeated at weekly intervals. The mixture causes superficial refrigeration with subsequent exfoliation. This exfoliation is the result of an inflammatory process, with varying amounts of edema. The therapeutic response is due to the repeated exfoliations. The term cryotherapy is

applied to this treatment. Forty-seven of the fifty patients were apparently either cured or greatly improved. Two patients failed to respond and one suffered a recurrence. Thirty-three were cured or greatly improved within four months. The other fourteen were equally benefited but required more than four months of treatment. Patients who had been cured by roentgen therapy showed further cosmetic improvement when cryotherapy was used solely with the aim of rendering the postacne scars and pits less conspicuous. Cryotherapy should be guardedly administered when there is atrophy of the skin even when a history of roentgen irradiation cannot be elicited from the patient. Perhaps more important than radiodermatitis is the presence of a melanotic nevus within the affected area or in its immediate vicinity. More than a superficial inflammatory reaction should not be set up. Exfoliation should not be repeated until the inflammation of the preceding treatment has subsided. The authors report the cures with considerable reservation, because no case has been observed for a sufficient length of time to warrant considering the cure permanent.

Archives of Surgery, Chicago

38: 979-1160 (June) 1939

Diaphragmatic Hernia in Infants: Report of Two Cases. E. M. Miller, A. H. Parmelee and H. N. Sanford, Chicago.—p. 979.
Lesions of Supraspinatus Tendon and Associated Structures: Investigation of Comparable Lesions in Hip Joint. M. T. Horwitz, Philadelphia.—p. 990.
Resection of Carcinomatous Rectosigmoid Juncture with Reestablishment of Intestinal Continuity: Preliminary Report. H. R. Arnold, San Francisco.—p. 1004.
*Carcinoma of the Lip: Clinical and Pathologic Study of 390 Cases, with Report of Five Year Cures. E. T. Newell Jr., Baltimore.—p. 1014.
Epulis: Series of Cases. B. G. Anderson, New Haven, Conn.—p. 1030.
*Possibility of Differential Section of Spinothalamic Tract: Clinical and Histologic Study. O. R. Hyndman and C. Van Epps, Iowa City.—p. 1036.
Functional Capacity of the Undescended Testis. C. E. Rea, Minneapolis.—p. 1054.
Routes of Absorption in Total Ureteral Obstruction. D. M. Morison, Edinburgh, Scotland.—p. 1108.
Effect of Experimentally Formed Tumors on Musculoskeletal System of the Rat. C. J. Sutro and L. Pomerantz, New York.—p. 1132.
Sixty-Eighth Report of Progress in Orthopedic Surgery. J. G. Kuhns, S. M. Roberts, W. A. Elliston, F. W. Ilfeld, G. G. Bailey, Boston; J. A. Freiberg, Cincinnati, and J. E. Milgram, New York.—p. 1150.

Carcinoma of the Lip.—Newell reviews 390 cases of carcinoma of the lip that were observed at the Johns Hopkins Hospital from 1900 to 1933. The diagnosis of carcinoma was made in every instance from sections, except in ten of the earlier cases (all cases of hopeless cancer). The lesions were generally well advanced. Besides affecting the percentage of five year cures unfavorably, delay in treatment shows the need for more prompt attention to lesions of the lip. The proportion of patients who showed metastasis or recurrence on first examination (36.4 per cent, or 143 of 390 patients) indicates the seriousness of delay in diagnosis and treatment. The average duration of symptoms was in excess of two years. The lesion first noticed by most of the patients was a small, painless ulcer, which at first grew slowly. Scabs often formed, and the lesion sometimes healed before a raw area reappeared. Frequently the patients stated that they had had fever blisters before but that this time the fever blister did not heal. The lesions usually became worse after the use of salves and mild caustics, although there was seldom any associated pain. Other early lesions noticed by the patients were warts, cracks, fissures, leukoplakia and chapping of the lips. There were 344 cases of squamous cell carcinoma, forty-four cases of basal cell carcinoma and two cases of adenocarcinoma. Only 2 per cent of the basal cell lesions occurred on the lower lip, and none of the adenocarcinomas. "Malignant wart" is a term used to indicate the papillary, squamous cell, low grade type of carcinoma. Clinically a lesion cannot always be diagnosed as benign or malignant. Emphasis is put on the microscopic study in relation to prognosis and therapy. Follow-ups were obtained in 328 of the 390 cases. The percentage of five year cures for the entire series was 61.6. The incidence of metastasis or recurrence on first examination was 36.4 per cent. Of 176 patients with no clinical evidence of metastases in whom local excision alone was performed there were 80.9 per cent with five year cures. The percentage of five year cures was 85.3 in those cases in which local excision plus dissection of the cervical glands was carried out but no metastasis found microscopically. Of eighty-three cases in which both local excision and cervical gland dissection were done but in which metastasis was found, the percentage of five year cures was 22.5. The operative mortality was 3.7 per cent in 349 cases; twelve deaths occurred in the last two groups of patients.

Section of Spinothalamic Tract.—In doing forty-one chordotomies during the last three years, Hyndman and Van Epps saw reason to question the accepted location of the spinothalamic tract as well as the accepted disposition of its fibers. They report six cases in which the operation was done with the patient under local anesthesia only. Sections were made in the cord according to various patterns, and cutaneous sensibility was tested at the operating table. Their conclusions are that the spinothalamic tract mediating the sensations of pain and temperature extends from a point about midway from the dentate ligament to the anterior roots to a point about midway from the anterior roots to the anterior median fissure. Hence a complete section should include this region. The region extending 2 mm. anterior to the dentate ligament contains no fibers conducting sensations of pain or temperature. As one progresses from the lower segments of the body upward, the corresponding "pain fibers" are disposed more and more anteriorly in the cord. It is possible, therefore, by differential section to eliminate the sensations of pain and temperature in the chest and to retain these modalities in the lower extremities.

Bulletin New York Academy of Medicine, New York

15: 357-424 (June) 1939

Genic and Hormone Factors in Biologic Processes. C. H. Danforth.—p. 359.
Clinical and Pathologic Aspects of Acute Leukemia. C. E. Forkner, New York.—p. 377.
Chronic Gastritis: Clinical Aspects. B. B. Crohn, New York.—p. 392.
Vitamin A, with Special Reference to Therapy. A. M. Yudkin, New Haven, Conn.—p. 406.

Canadian Public Health Journal, Toronto

30: 219-268 (May) 1939

Possibilities and Limitations of Full-Time Health Services. W. A. McIntosh, New York.—p. 219.
Development of Public Health in Nova Scotia. P. S. Campbell and H. L. Scammell, Halifax, N. S.—p. 226.
Heart Disease and Cancer Mortality Trends: Part II. Mary A. Ross and N. E. McKinnon, Toronto.—p. 239.
Gonococcus Culturing in Public Health Laboratory Practice. Mabel M. Malcolm and C. E. Dolman, Vancouver, B. C.—p. 252.

Delaware State Medical Journal, Wilmington

11: 71-132 (May) 1939

Our Children. M. A. Tarumianz, Farnhurst.—p. 71.
*Male Hormone Therapy of Male Climacteric and Gonadal Insufficiency State. C. W. Dunn, Philadelphia.—p. 76.
Fatal Hemorrhagic Shock Following Neoarsphenamine: Report of Case. I. J. Wolman, Philadelphia, and P. F. Elfeld, Farnhurst.—p. 84.
Metrazol. J. W. Ballard, Farnhurst.—p. 86.
The Hazards of Classification: Illustrating the Loss of Appreciation of Behavior Factors Liable in Snapfast Diagnoses. C. Uhler, Farnhurst.—p. 90.
Metrazol Therapy in Psychoses of Doubtful Diagnosis. B. G. Lawrence, Farnhurst.—p. 93.
Myelomatosis: Clinical Observation. G. J. Gordon, Farnhurst.—p. 97.
The Need for Reorientation in the Classification of the Endocrinopathies. Fredericka F. Freytag, Farnhurst.—p. 99.
Metrazol Treatment. M. Zimbler, Farnhurst.—p. 101.
Clinical Contribution to Study of Pharyngeal Myoclonus. G. J. Gordon and E. Kelemen, Farnhurst.—p. 107.
Orientation in Use of Sulfanilamide and Its Allied Compounds. G. S. Bieringer, Farnhurst.—p. 108.

Androgen for Male Climacteric and Gonadal Insufficiency.—Dunn treated fifteen cases of gonadal insufficiency with testosterone propionate. There were five cases of eunuchoidism, two of testicular hypoplasia, two of testicular atrophy following mumps, two secondary to anterior pituitary deficiency (one with infantilism and one with cryptorchidism) and four of the climacteric. The results of the treatment showed, in general, a relief of symptoms proportionate to the dosage administered. The treatment was effective in relieving the nervous and mental symptoms associated with the hypogonadal syndrome. The dosage required varied with the degree of gonadal

deficiency; from 30 to 150 mg. weekly, administered hypodermically, gave the best results. As the therapy is one of replacement, symptoms may recur when the deficiency state recurs. Percutaneous application of testosterone propionate in hydrous wool fat shows evidence of effective absorption of the male hormone by the manifestations of increased hirsuties and a general constitutional effect. Its present strength does not appear adequate to relieve the symptom state. The increase in physical energy, as well as the ability to sustain physical effort over a greater period of time, was marked. There was a greater mental ability not only in concentration but in the fulfilling of social and economic responsibilities. There is, first, a mental quietude and repose replacing the previous irritability and, later, as the energies improve, there is increased interest in business and social activities. When neurocirculatory symptoms are present, their abatement contributes materially to the mental and physical improvement. It is not always possible to obtain rapid therapeutic effects, even by hypodermic administration of the testosterone propionate. Accordingly, the author believes that proper sedation has a field of application during the early acute clinical conditions, but as soon as a sufficient amount of the compound has been given the sedation should be reduced and later discontinued.

Endocrinology, Los Angeles

24: 763-904 (June) 1939

*Clinical Use of Synthetic Male Sex Hormone. H. H. Turner, Oklahoma City.—p. 763.
*Treatment of Addison's Disease with Adrenal Cortex Extract. W. O. Thompson, Phebe K. Thompson, S. G. Taylor 3d and W. S. Hoffman, Chicago.—p. 774.
Influence of Some Ductless Glands on Metabolic Processes. E. C. Kendall, Rochester, Minn.—p. 798.
Stimulating Action on Metabolism and Heart Beat of Various Thyroid Preparations, Determined in the Thyroidectomized Rat. A. E. Meyer and Marcella Yost, Brooklyn.—p. 806.
Interactions of Estrone and Prolactin, with Special Reference to Effect of Estrone on Pigeon Crop-Gland Response. S. J. Folley, Reading, England.—p. 814.
Inhibition of Action of Follicle Stimulating Hormone by Pituitary. H. L. Fevold and Virginia Mayo Fiske, Cambridge, Mass.—p. 823.
Effect of Local Application of Progesterone on Rabbit Uterus. D. A. McGinty, L. P. Anderson and N. B. McCullough, Detroit.—p. 829.
Excretion of Urinary Androgens Following Injection of Testosterone Propionate. E. P. McCullagh, J. M. Rumsey and W. K. Cuyler, Cleveland.—p. 833.
Arrhenoblastoma Which Simulated Cushing's Disease: Case. C. K. Canelo and H. Lisser, San Francisco.—p. 838.

Clinical Use of Synthetic Male Sex Hormone.—Turner used synthetic male sex hormone, testosterone propionate, in the treatment of fifty-four patients (from 7 to 70 years of age) with various types of genital anomalies and dysfunctions, which included adult hypogonadism, sexual diminution associated with senescence, adiposogenitalism, gynecomastia and benign prostatic hypertrophy. In doses of from 10 to 75 mg. weekly the hormone was found effective in every hypogonad case, as evidenced by promoting hair and penile growth, producing erections and emissions, developing the libido and potentia coeundi and by generalized changes in secondary sex characteristics. Gynecomastia with normal secondary sex development is apparently not influenced by injections of the hormone. The androgen brought about considerable relief of the subjective symptoms of sexual diminution associated with senescence, and in cases of benign prostatic hypertrophy, as shown by the clinical improvement in the usual symptoms and signs of prostatic obstruction. No untoward by-effects occurred in any of the cases treated.

Adrenal Cortex Extract for Addison's Disease.—During the last three and a half years Thompson and his associates observed the effect of the prolonged administration of adrenal cortex extract in seven patients with marked Addison's disease, varying in age from 18 to 49 years. All of them showed the typical clinical signs of the disease, including pigmentation, reduction in blood pressure and characteristic chemical alterations in the blood. In two patients active tuberculosis was present. Of the seven patients, four are now living and three are dead. It would appear that with adequate doses of extract patients may be maintained in a sufficiently satisfactory condition to carry on normal activity, provided no active tuberculous infection is present. The smallest dose that has ever accomplished this purpose is 10 cc. daily by the subcutaneous route, and usually much more is required. The addition of sodium salts does not improve the condition of the patient if an adequate amount of extract is administered. The authors believe that their patients would all probably have been in better health if they had been able to administer three or four times as much extract as they did. The failure of the pigmentation to disappear completely and the tendency of the concentration of total base in serum to remain at or just below the lower level of normal appear to confirm this point of view and suggest that with the doses that they were able to administer they had only partially controlled the deficiency. Their experience convinces them that with sufficiently large doses of extract many patients with Addison's disease may be kept completely well. Every patient with Addison's disease should be under constant observation of a physician in order that emergencies may be treated as soon as they arise. Only in this way can unnecessary deaths be avoided. Patients should be instructed to begin sodium salts and cortical extract in large doses at the first sign of an impending crisis. Infections of all types should be avoided and every infection that does occur should be regarded as an emergency. In a crisis it is important to begin treatment at once, as delay may be fatal, to administer intravenously 10 cc. of an active adrenal cortex extract and about 170 cc. of a 5 per cent solution of dextrose in physiologic solution of sodium chloride every hour, until vomiting stops and appetite returns. There is no danger at present of giving an overdose of extract. Early in a crisis a patient may be revived by extract alone. The maintenance dose of the extract (at least 10 cc. daily) should be increased during an infection. If no active tuberculosis is present, patients may be maintained in a satisfactory condition for long periods. There appears to be some relationship between the nutritional state of the patient and the level of the blood pressure. When the basal metabolism is low, raising it to normal with a suitable dose of thyroid is an important part of the treatment. Under such circumstances no aggravation of the disease has been observed from its use. There appears to be a relationship between the function of the ovary and the adrenal cortex.

Florida Medical Association Journal, Jacksonville

25: 537-592 (May) 1939

The "Surgical Kidney" in Obstetrics. R. B. McIver, Jacksonville.—p. 549.
Treatment of Chronic Prostatitis by Injection. P. D. Melvin, Miami.—p. 554.
The Insured Neurotic. W. C. McConnell, St. Petersburg.—p. 556.
Diagnosis and Treatment of Sterility. E. B. Woods, Tampa.—p. 558.
Foreign Bodies of Cornea, Their Removal and Subsequent Treatment. C. E. Dunaway, Miami.—p. 565.
Maxillary Sinusitis Associated with Dental Caries. J. N. McLane, Pensacola.—p. 566.
Prontosil in Treatment of Malaria: Case Report. E. C. Chamberlain, Fort Lauderdale.—p. 569.

Johns Hopkins Hospital Bulletin, Baltimore

64: 279-368 (May) 1939

Idiopathic Familial Lipemia. L. E. Holt Jr., F. X. Aylward and H. G. Timbres, Baltimore.—p. 279.
Follicular Lymphoblastoma and Related Form of Lymphosarcoma. S. Mayer Jr. and H. M. Thomas Jr., Baltimore.—p. 315.
*Treatment of Addison's Disease with Pellets of Crystalline Adrenal Cortical Hormone (Synthetic Desoxycorticosterone Acetate) Implanted Subcutaneously. G. W. Thorn, R. P. Howard, K. Emerson Jr. and W. M. Firor, Baltimore.—p. 339.

Adrenal Cortical Hormone for Addison's Disease.—In the treatment of six cases of Addison's disease, Thorn and his collaborators implanted subcutaneously pellets of crystalline desoxycorticosterone acetate. None of these patients could be maintained in good condition by means of sodium chloride therapy alone. Sodium chloride therapy was continued in five of the six cases, as it has been shown that it greatly reduces the necessary dose of desoxycorticosterone acetate. A diet of constant mineral intake was provided. The daily maintenance dose of desoxycorticosterone acetate in sesame oil, injected once daily, was determined. The maintenance of optimal body weight, normal blood pressure, normal plasma volume, positive sodium and chloride balance and normal concentration of plasma electrolytes was regarded as evidence of adequate treatment. Daily injections of the hormone in oil were then discontinued and, under local anesthesia, pellets of crystalline desoxycorticosterone acetate, weighing from 50 to 150 mg. each, were inserted subcutaneously in the infrascapular region. The implantation of

pellets occasioned no untoward reaction. Striking and continued improvement followed the implantation in all the cases. The changes were similar to those previously observed following a daily injection of the hormone in oil. In one case in which the dextrose tolerance curve was abnormal, continued treatment with pellet implants was associated with a marked change toward normal. Pellets of synthetic hormone are slowly absorbed and thus exert a prolonged effect. Implantation of the pellets obviates the necessity for the daily injection of the hormone and, in addition, effects a great economy of the hormone. Pellets weighing from 50 to 150 mg. are absorbed at a rate of from 0.25 to 0.35 mg. a day. It is desirable to insert pellets of a standard size of from 125 to 150 mg., obtaining varying concentrations of hormone by increasing or decreasing the number of pellets rather than by varying the size. The maintenance of a rather constant rate of absorption as a pellet decreases in size is probably accounted for by either a softening of the pellet, which would result in more rapid absorption, or canalization, which would offer a greater surface for absorption. The fact that a prolonged period exists during which absorption is so constant greatly favors the practical applicability of this technic.

Journal of Experimental Medicine, New York

69: 755-904 (June) 1939

Antigen-Antibody Reactions Between Layers Adsorbed on Built Up Stearate Films. E. F. Porter, Cambridge, Mass., and A. M. Pappenheimer Jr., Jamaica Plain, Mass.—p. 755.
Studies on Sensitization of Animals with Simple Chemical Compounds: VI. Experiments on Sensitization of Guinea Pigs to Poison Ivy. K. Landsteiner and M. W. Chase, New York.—p. 767.
Electrophoresis of Anterior Pituitary Proteins. R. A. Shipley, K. G. Stern and A. White, New Haven, Conn.—p. 785.
Epidemiology of Lymphocytic Choriomeningitis in Mouse Stock Observed for Four Years. E. Traub, Princeton, N. J.—p. 801.
Osmotic Pressure Study of Protein Fractions in Normal and in Nephrotic Subjects. J. Bourdillon, New York.—p. 819.
Experimental Hypertension: Effects of Unilateral Renal Ischemia Combined with Intestinal Ischemia on Arterial Blood Pressure. A. Blalock, S. E. Levy and R. D. Cressman, Nashville, Tenn.—p. 833.
Serologic Studies of Swine Influenza Viruses. R. E. Shope, Princeton, N. J.—p. 847.
*Amount and Duration of Immunity Induced by Intradermal Inoculation of Cultured Vaccine Virus. T. M. Rivers, S. M. Ward and R. D. Baird, New York.—p. 857.
Protective Antibodies in Serum of Syphilitic Rabbits. T. B. Turner, Baltimore.—p. 867.

Immunity to Vaccine Virus.—Rivers and his colleagues studied a large group of children in order to obtain more complete information concerning the amount and duration of immunity produced by cultured vaccine virus against the New York City calf lymph strain of virus. In addition, the immunity produced by cultured virus against other strains of calf lymph vaccine virus and the differences that the manner of performing primary inoculations with cultured virus have on subsequent immunity are considered. The 331 children who had received one inoculation of cultured virus resulting in a primary take from one month to three years and nine months previously were revaccinated with New York City calf lymph virus and eighty-two of these, 25 per cent, responded with immune reactions, while 249, or 75 per cent, showed accelerated takes. Analysis of the data revealed that the proportion of immune individuals was fairly constant and bore no relation to the interval which had elapsed between the primary vaccination with cultured virus and revaccination with calf lymph. The percentage of accelerated reactions was slightly higher in the children revaccinated after one year and the reactions were more severe in this group, but little indication is had that susceptibility to calf lymph virus increased with the lapse of time within the limits of the observations. The differences in the age at which the primary vaccinations were performed had no influence on the proportion of children who retained complete immunity during the period of observation. Seventy-eight of the 331 children who were revaccinated with New York City calf lymph received at the same time an inoculation with commercial calf lymph virus (A) and another group of eighty-two children received in addition to New York City virus an inoculation of commercial calf lymph virus (B). Of the seventy-eight children seventeen responded with immune reactions to New York City virus, while fifty-six responded with immune reactions to virus A; of the eighty-two children twenty-nine were immune to New York City virus, while forty-five responded in that manner to calf lymph B. Sixty-six children whose records showed that they had had two successful simultaneous primary vaccinations were revaccinated dermally with New York City calf lymph from two to six months later. Eighteen responded with immune reactions, while forty-eight showed accelerated takes. Comparison of these figures with those obtained in the 331 children who received only a single injection of cultured virus for primary vaccination shows that the introduction of a double amount of this virus and the production of two primary lesions instead of one did not alter the percentage of children who retained for six months complete immunity to the New York City calf lymph. The authors suggest that primary vaccinations be made intradermally with their cultured virus and that revaccinations be made dermally from six months to a year later by means of a potent calf lymph virus. In this way vaccinated individuals will not become sick and will not be subjected to the dangers associated with primary vaccinations with calf lymph virus but will obtain a solid and lasting immunity to smallpox. Fifty-four children were inoculated intradermally with the cultured virus and from two to six months later they were reinoculated dermally with the New York City calf lymph virus. Twenty-one of these responded with accelerated takes, while thirty-three showed immune reactions. The accelerated takes were mild and healed quickly, leaving only small superficial scars.

Journal-Lancet, Minneapolis

59: 249-286 (June) 1939

Significance of Antenatal Care in Reducing Maternal Mortality. F. L. McPhail, Great Falls, Mont.—p. 249.
Fractures of Spine and Pelvis. A. F. O'Donoghue, Sioux City, Iowa.—p. 252.
The Work of a University Psychiatric Clinic. R. Fleming, Boston.—p. 258.
Are Herniorraphies as Successful as They Should Be? R. W. McNealy, Chicago.—p. 262.
The Hygiene of Physical Education Activities. T. A. Storey, Palo Alto, Calif.—p. 264.
Gonococcus Cultures as Aid to Diagnosis. L. H. Winer and A. Leibovitz, Minneapolis.—p. 267.
Lobectomy and Pneumonectomy for Lung Suppuration and Malignancy: Comprehensive Analysis Including the Authors' Series. F. S. Dolley and J. C. Jones, Los Angeles.—p. 268.
Male Hormone Therapy of Prostatic Hypertrophy. M. Meltzer, New York.—p. 279.

Kentucky Medical Journal, Bowling Green

37: 223-268 (June) 1939

What Has Happened to Massage? F. Becker, Harrodsburg.—p. 223.
Management of Lesions of Colon and Rectum. F. H. Lahey, Boston.—p. 232.
Treatment of Diarrhea in Infants. Caroline P. Scott, Lexington.—p. 240.
Treatment of Pneumonia. A. T. Hurst, Louisville.—p. 243.
Bronchial Asthma. F. A. Simon, Louisville.—p. 250.
Practical Application of the Electrocardiogram. J. M. Kinsman, Louisville.—p. 255.

Missouri State Medical Assn. Journal, St. Louis

36: 225-260 (June) 1939

Prostatic Hypertrophy: Factors Determining Management of Patients. A. L. Stockwell and C. K. Smith, Kansas City.—p. 225.
Diseases of Testicle. O. J. Wilhelmi, St. Louis.—p. 229.
Indications for Surgery of Stomach. J. H. Hershey, St. Louis.—p. 230.
Radical Surgical Resection for High Lying Malignant Lesions of Stomach. C. J. Hunt, Kansas City.—p. 233.
Ependymoma: Case Study. H. M. Gilkey and W. E. Owen, Kansas City.—p. 236.
Staphylococcic Cellulitis of the Face: Prophylactic Treatment with Report of Cases. L. Scarpellino and P. F. Stookey, Kansas City.—p. 239.
Myasthenia Gravis: Recent Developments in Treatment: Report of Case. A. B. Day, St. Louis.—p. 243.
*Epilepsy and Hypertensive States: Bilateral Carotid Denervation. R. F. Pittam, Kansas City.—p. 245.
Has the Medical Profession Failed in Its Obligation to Society? D. F. Manning, Marshall.—p. 248.

Epilepsy and Hypertensive States.—Having observed that headaches of migraine-like severity often accompany grand mal attacks or are found in the family of the epileptic patient, Pittam is of the opinion that spasm of cerebral vessels is probably the factor responsible. This does not explain the discharge of energy but, because in certain cases he has been able to control spasm in vessels of the extremities by the interruption of reflex pathways within the wall of the vessel itself, he felt that if he could do the same in the intricate plexuses of the carotid arteries it would be possible to affect the visible or objective

features of so-called epilepsy. Seven cases of epilepsy with good results in five, following carotid denervation, are reported. In three cases of hypertension with different symptoms the results of carotid denervation were also good.

New England Journal of Medicine, Boston

220: 819-858 (May 18) 1939

Strangulated Hernia: Report of Two Cases in Which the Sac Was Found in an Unusual Location. J. E. Dunphy, Boston.—p. 819.
Female Sex Hormones. R. T. Frank, New York.—p. 821.
Present Status of Blood Sedimentation Rate. A. S. Johnson, Springfield, Mass.—p. 823.
Electrolyte and Water Balance. A. M. Butler, Boston.—p. 827.

220: 859-900 (May 25) 1939

Biopsy of the Uterine Cervix: End Results of 100 Consecutive Interventions. L. E. Phaneuf and M. O. Belson, Boston.—p. 859.
Group Hospitalization. R. F. Cahalane, Boston.—p. 861.
*Testosterone Propionate as Therapeutic Agent in Patients with Organic Disease of Peripheral Vessels: Preliminary Report. E. A. Edwards, Boston; J. B. Hamilton, New Haven, Conn., and S. Q. Duntley, Cambridge, Mass.—p. 865.
Otolaryngology. C. G. Flake, Boston.—p. 866.

Testosterone Propionate for Vascular Disease.—Edwards and his associates make a preliminary report on the effect of crystalline testosterone propionate in the treatment of seven male patients suffering from organic vascular disease. Three of the men presented typical signs of thrombo-angiitis obliterans and the other four were arteriosclerotic. In all seven patients the involvement was major, with loss of the popliteal, femoral and, in one case, the iliac pulsations. The signs and symptoms were marked, including small ulcerations in two of the patients with thrombo-angiitis obliterans. The testosterone propionate, dissolved in peanut oil, was given intramuscularly two or three times a week. Adjunctive treatment consisted only of general hygiene, except in the ulcer-free patient with thrombo-angiitis obliterans, who received eight hours of suction-pressure treatment. None of the patients have been followed for more than several months, as treatment of the first patient was started on July 23, 1938. Each of the patients showed a lack of skin arterialization by spectrophotometry which involved not only the diseased limbs but also the entire body. The administration of testosterone propionate showed an early and decided arterialization of the cutaneous blood. Moreover, the after-treatment curves likewise showed an inconstant diminution in the volume of blood in the more venous areas of the body. Other objective evidence of favorable change was an increase in the systolic pressure of from 6 to 26 mm. of mercury in the hypotensive members of this group and a lowering of hypertension in two cases. The ulceration in one patient with thrombo-angiitis obliterans has healed; the second has greatly improved. There was marked improvement in the walking ability of all the patients, with delay or abolition of intermittent claudication. Two patients were no longer subject to night pain, which had troubled them previously. Subjectively, the patients reported an increased activity and a feeling of optimism, results similar to those reported previously with this treatment.

New Jersey Medical Society Journal, Trenton

36: 347-406 (June) 1939

The Problem of the Drinking Driver. R. A. Kilduffe, Atlantic City.—p. 353.
Health Survey of Paterson Relief Clients in 1938. F. P. Lee and W. J. Grosfeld, Paterson.—p. 356.
Abdominal Surgery in Infancy and Childhood. T. H. Lanman, Boston.—p. 360.
Modern Concepts of Etiology of Peptic Ulcer and Their Bearing on Therapy. G. B. Eusterman, Rochester, Minn.—p. 369.
Case of Tetanus. N. Manning, Amboy.—p. 379.

New York State Journal of Medicine, New York

39: 1055-1166 (June 1) 1939

Thyroid Disorders: VIII. Operability of the Hyperthyroid Patient as Indicated by Responses to Operation. E. Goetsch, Brooklyn.—p. 1059.
Diphtheria of Pleura. W. J. Davies, Rockville Centre.—p. 1084.
Clinical Significance of Prerenal Azotemia in Digestive Tract Disease. H. A. Rafsky and M. Weingarten, New York.—p. 1086.
Impetigo Contagiosa Complicated by Acute Nephritis. S. H. Silvers, Brooklyn.—p. 1093.
Industrial Epididymitis and Epididymo-Orchitis. G. E. Slotkin, Buffalo.—p. 1096.
Study of Sixty-Three Patients Before and After Weight Reduction. E. C. Beck and R. S. Hubbard, Buffalo.—p. 1102.
Electrocardiography: Values and Limitations. H. Tarnower, Scarsdale.—p. 1108.
Administrative Medicine. E. Emerson, New York.—p. 1115.

Oklahoma State Medical Assn. Journal, McAlester

32: 161-190 (May) 1939

Medical Objectives. W. A. Howard, Chelsea.—p. 161.
Injuries of Brain and Spinal Cord. F. L. Flack, Tulsa.—p. 166.
Diphtheria Carriers. E. H. Coachman, Muskogee.—p. 170.
Some Observations on Diagnosis and Treatment of Pneumonias During Infancy and Childhood. C. W. Arrendell, Ponca City.—p. 172.
Bilharzia: Report of Case. E. S. Sullivan, Oklahoma City.—p. 175.
Common Skin Diseases of Lower Extremities. W. A. Showman, Tulsa.—p. 177.

Philippine Islands Med. Association Journal, Manila

19: 195-268 (April) 1939

Nature of Bacteriophage from Point of View of New Chemical Concept, Its Action and Role: Condensed Report. J. F. Leyva and P. I. De Jesus, Manila.—p. 195.
Pharmacopeial Doses and the Physician. R. Guevara, Manila.—p. 207.
Medicinal Lizards in the Philippines. E. Y. Garcia and D. K. Villalus, Manila.—p. 217.
Industrial Compensation Law and Emergency Law Considerations. F. O. Smith, Fabrica.—p. 225.
Place of Health Education in Public Health Program. C. E. Turner, Cambridge, Mass.—p. 231.

Public Health Reports, Washington, D. C.

54: 815-856 (May 19) 1939

Organized Public Nursing and Variation of Field Programs in Ninety-Four Selected Counties. J. W. Mountin and Evelyn Flook.—p. 815.
Maternal Services in Michigan, with Special Reference to Economic Status. Jennie C. Goddard and C. E. Palmer.—p. 825.
Notes on Fleas of Prairie Dogs, with Description of a New Subspecies. W. L. Jellison.—p. 840.

54: 857-918 (May 26) 1939

Prevalence of Poliomyelitis in the United States in 1938. C. C. Dauer.—p. 857.
Domestic Water and Dental Caries, Including Certain Epidemiologic Aspects of Oral Lactobacillus Acidophilus. H. T. Dean, P. Jay, F. A. Arnold Jr., F. J. McClure and E. Elvove.—p. 862.
Early State Hospitals for Seamen: The First in America Provided by the State of Virginia, the Second, Some Years Later, by Massachusetts. J. W. Trask.—p. 888.
*Dermatitis and Coexisting Fungous Infections Among Plate Printers. P. A. Neal and C. W. Emmons.—p. 892.

54: 919-968 (June 2) 1939

Health Needs of the Nation. T. Parran.—p. 919.
Studies of Sewage Purification: X. Changes in Characteristics of Activated Sludge Induced by Variations in Applied Load. C. C. Ruchhoft and R. S. Smith.—p. 924.
Study of Human Serums Antibodies Capable of Neutralizing Virus of Lymphocytic Choriomeningitis. J. G. Wooley, F. D. Stimpert, J. F. Kessel and C. Armstrong.—p. 938.
Acute Response of Guinea Pigs to Inhalation of Dimethyl Ketone (Acetone) Vapor in Air. H. Specht, J. W. Miller and P. J. Valaer.—p. 944.

Dermatitis and Fungous Infections Among Plate Printers.—Neal and Emmons studied the cutaneous lesions that occurred in a large printing establishment. There were 1,091 employees in the establishment. Of these, 378 had a severe exposure to inks and cleaning materials. The majority of the diseases occurred among these 378 men. In cleaning the hands, all printers from a given section washed in a common sink containing light mineral oil. Soap, stiff brushes, potassium carbonate, sand and paper towels were other cleaning agents used, and each man used one or more of these materials. Of the 365 men examined, sixteen had lesions which were classified as being of a chronic, eczematous, vesicular type; two had lesions of a chronic dry eczematous type; eight had, or showed evidence of having had, a folliculitis; three had lesions of a chronic, eczematous, fissure type, and three had evidence of dermatophytids. The duration of the dermatitis varied from one to thirty years. In most cases the lesions cleared when the patient avoided exposure to inks and cleaning materials and reappeared when he returned to work. Thirty-seven men whose hands were free from dermatitis at the time of examination had a past history of dermatitis of the hands. It was estimated that the total loss of working time because of dermatitis of the hands was thirteen years for one man during the period from 1910 to 1936. No dermatophytes were found by direct examination or by culture on the hands of any of the men with dermatitis, but they were found in cultures made from scrapings from the feet. There was no significant difference in the incidence of dermatophytosis of the feet in men with present evidence or past history of dermatitis of the hands and in those men not exposed to inks or without dermatitis. Men (121) exposed to inks (with or without dermatitis) and twenty-four controls were patch tested to inks and their component parts. Thirteen of the men exposed to inks gave positive reactions. No positive tests were obtained

among seventy patch-test controls. Of the plate printers tested who had dermatitis at the time of examination 50 per cent gave positive reactions. Of the plate printers with a past history of dermatitis of the hands 12.1 per cent gave positive reactions. Results of the patch tests with component parts of inks were variable. Recommendations for the control of the dermatitis include preemployment examinations and the exclusion from certain occupations of persons with a history of allergic disorders, constitutional conditions predisposing to cutaneous diseases and seborrheic disorders of the skin; periodic medical examinations to determine the incidence and cause of cases of dermatitis appearing in the plant; protective measures, proper materials and methods for cleansing the hands and full cooperation of the employees, and the provision of appropriate sanitary measures.

Rhode Island Medical Journal, Providence

22: 89-112 (June) 1939

Surgery in Treatment of Disorders of Autonomic Nervous System. S. J. Goldowsky, Providence.—p. 89.

Rocky Mountain Medical Journal, Denver

36: 369-440 (June) 1939

Acute Abdominal Emergencies. I. Abell, Louisville, Ky.—p. 386.
Present Status of Surgical Treatment of Duodenal Ulcer. K. B. Castleton, Salt Lake City.—p. 394.
*Hypothyroidism as Factor in Menstrual Disturbances and Sterility. L. W. Mason, Denver.—p. 399.
X-Ray Pelvimetry. J. H. Spillane Jr., Colorado Springs, Colo.—p. 403.
Conservative Management of Antepartum Accidental Hemorrhage. J. B. Farley, Pueblo, Colo.—p. 408.

Hypothyroidism in Menstrual Disorders and Sterility.—Mason asserts that a normal female sex cycle is dependent on the normal functioning of all the endocrine glands. This delicate hormone balance may be upset by an abnormal function of any one gland which is part of the chain. He particularly discusses the thyroid and says that hypothyroid states of far less degree than those of the typical textbook picture may be the cause of profound alterations in the female sex cycle, in which only one or two, or perhaps not any, of the textbook signs are present. In such cases the basal metabolism may be significantly low or it may be well within normal limits, and the diagnosis of hypothyroidism substantiated by the benefit to the patient of thyroid therapy. Rather than infrequent and scanty menstruation, combined with varying periods of amenorrhea, it has been the author's experience and that of others to find this relatively infrequently compared to the other extreme; viz., shortened menstrual intervals and menorrhagia. Frequently the bleeding is continuous, all rhythm being lost. Especially is this seen in the adolescent girl. By keeping the probability of hypothyroidism in mind as the etiologic factor in menstrual abnormalities, when gross pelvic pathologic conditions are absent, one can in most instances elicit other points which further direct attention to the thyroid. The one most commonly found is easy fatigability. Often a patient who has suffered from menorrhagia for months or years attributed her chronic exhaustion to the long continued excessive loss of blood. Unfortunately the doctor frequently does also and thereby misses the cue in diagnosis and treatment. Hypothyroidism is more frequent than is generally supposed. A thorough interest in the thyroid should be part of the study of every case of sterility, menstrual difficulty or recurrent abortions. Many cases of relative infertility and spontaneous abortions can often be explained on the basis of hypothyroidism, and this need not be of severe grade, that is an underlying endocrine imbalance. The administration of thyroid may safely be tried in all cases of menstrual disturbances when local pelvic causes cannot be found, when the basal metabolism rate is not significantly high, or in the absence of obvious signs or symptoms of hyperthyroidism. The chief guide to such treatment is the patient's response.

South Carolina Medical Assn. Journal, Greenville

35: 135-162 (June) 1939

General Problem of Thymus Gland. G. D. Johnson, Spartanburg.—p. 135.
Meckel's Diverticulum with Subsequent Intestinal Obstruction. B. J. Workman, Woodruff.—p. 139.
Few Brief Remarks on Stones in Ureter. S. A. Kirkland, Atlanta, Ga.—p. 141.
Poliomyelitis in Charleston in 1939. J. I. Waring, Charleston.—p. 156.

Surgery, Gynecology and Obstetrics, Chicago

68: 979-1126 (June) 1939

*Surgical Treatment of Chronic Constrictive Pericarditis. G. J. Heuer and H. J. Stewart, New York.—p. 979.
Squamous Cell Carcinoma of Extremities. H. Charache, Brooklyn.—p. 1002.
Present Status of Chronic Osteomyelitis. H. R. McCarroll and J. A. Key, St. Louis.—p. 1007.
Bacteriologic Study of Peritoneal Fluid in Perforated Peptic Ulcers. M. Davison, L. J. Aries and I. Pilot, Chicago.—p. 1017.
Use of Neosynephrine in Spinal Anesthesia. R. S. Brunner and G. de Takats, Chicago.—p. 1021.
*Knee Joint Tuberculosis: *222* Patients Treated by Operative Fusion. J. W. Toumey Jr., New York.—p. 1029.
Phosphatase Determination in Differential Diagnosis of Bone Lesions. C. C. Franseen, C. C. Simmons and Regina McLean, Boston.—p. 1038.
Experiments Concerning Ligation and Refrigeration in Relation to Local Intoxication and Infection. F. M. Allen, New York.—p. 1047.
Analysis of Immediate Postoperative Complications in 2,000 Cases of Inguinal Hernia. F. Beekman and J. E. Sullivan, New York.—p. 1052.
Reconstruction Operation for Adenomatous Disease of Prostate. C. Morson, London, England.—p. 1060.
Burn Contractures of Hand. H. M. Blackfield, San Francisco.—p. 1066.
Technical Notes on Hypertrophic Pyloric Stenosis. S. J. Seeger, Milwaukee.—p. 1074.
Extraperitoneal Implantation of Colon: One Stage Resection for Carcinoma. W. T. Harsha and W. T. Harsha Jr., Chicago.—p. 1077.
Walking Iron for Immediate Use on Wet Plaster Casts. B. B. Larsen, Cleveland.—p. 1082.
Surgical Aspects of Neurogenic Tumors of Abdomen. V. L. Schrager, Chicago.—p. 1085.
Injection Treatment of Hernia. H. O. Wernicke, Chicago.—p. 1093.
Operative Treatment of Pes Planus. C. S. Young, Los Angeles.—p. 1099.

Chronic Constrictive Pericarditis.—Heuer and Stewart discuss nine cases of chronic constrictive pericarditis. Seven of the nine patients were subjected to operation. It was found that the arteriovenous oxygen difference was increased, the venous pressure was elevated and the circulation time was prolonged, while the cardiac output per minute, the stroke volume and the cardiac index were diminished. These values tended to, or actually did, return to normal. The clinical manifestations of this syndrome have been well described by White. The diagnosis of chronic constrictive pericarditis should be considered in the presence of signs of congestive heart failure not associated with the common etiologic causes. Patients with pericardial effusion in the absence of rheumatic heart disease should be kept under observation in order to detect the development of constrictive pericarditis. Tuberculosis as a cause of the disease was proved in only one of the seven cases in which operation was performed. While the results of surgical treatment undoubtedly are striking, a study of the surgical cases as reported in the literature shows that the primary mortality following decortication of the heart is still high (33 per cent). Of the 143 cases collected from the literature by the authors (exclusive of their own), death occurred in nineteen on the operating table and in twenty-eight during the immediate postoperative period. All seven patients with chronic constrictive pericarditis subjected to pericardiectomy have recovered. Three patients are cured in the sense that their symptoms and signs have disappeared and they are able to lead normal active lives, three patients are markedly improved and one patient is improved although sufficient time has not elapsed to make an accurate evaluation of the results of operation.

Knee Joint Tuberculosis.—Toumey states that from September 1915 to December 1936 knee fusion was performed in *222* cases of tuberculosis of the knee joint at the New York Orthopedic Dispensary and Hospital. Of these cases 199 have been followed from one to seventeen years after operation with an average follow-up period of five and one-half years. Fusion occurred in 196 of these cases. Fusion took place and the plaster cast was dispensed with at an average period of eight months after operation. The disease subsided in all but seven, in which sinuses persisted. Tuberculosis did not recur in any of the knee joints in which fusion took place. Fifty-nine patients were 10 years of age or less at the time of operation and fourteen were 5 years old or less. On the basis of his experience with operative arthrodesis of the knee joint for tuberculosis the author recommends this procedure for both children and adults. In no other joint in the body has such a high percentage of successful fusions been obtained.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

51: 197-250 (May) 1939

Some Clinical Manifestations of Endogenous Sensitization Eruptions Following Local Infection or Injury. W. H. Brown.—p. 197.

British Journal of Ophthalmology, London

23: 289-368 (May) 1939. Partial Index

Solitary Retinochoroiditis, with Reference to Retinochoroiditis Juxtapapillaris—Jensen. C. Heath.—p. 289.

Therapeutic Experiments in Cases of Retinitis Pigmentosa. I. Biró.—p. 332.

Epithelial Inlay with Kerr-Material to Form an Eye Socket. Ida Czukrász.—p. 343.

Primary Lues in Superior Fornix: Case. Ida Czukrász.—p. 347.

British Medical Journal, London

1: 857-906 (April 29) 1939

Pelvic Disproportion: Historical—Classification—Diagnosis. J. M. M. Kerr.—p. 857.

Occupational and Economic Factors of Mortality. M. Greenwood.—p. 862.

Nature of Chronic Mastitis. H. J. B. Atkins.—p. 866.

Blood Levulose in Levulose Tolerance Test, with Special Reference to Normal Standards. Freda K. Herbert.—p. 867.

*Asthma as Sequela of Nasal Injury. W. A. Bourne.—p. 870.

Management of a Hay Fever Ionization Clinic: Comparative Statistical Survey of Results in 1937 and 1938. P. Franklin.—p. 871.

Asthma as Sequela of Nasal Injury.—Bourne asserts that nasal injury resulting in deformity was the precipitating factor in the development of asthma in two patients who had never previously shown any asthmatic tendency and have shown none in the considerable time that has elapsed since full recovery from operative repair. On the other hand, the great majority of cases of nasal injury have no sequela of this kind. A number of reasons may be suggested for the appearance of asthma in these two individuals. Doubtless unknown predisposing factors were present. In addition, the accidents produced severe trauma. The violence with which the girl struck the ground and the man the windshield was probably more than is involved in most nasal accidents. There was also an element of psychic trauma. Shock at the time, the possibility of police intervention, litigation in the civil courts and anxiety regarding means of livelihood were added. Further, and it is suggested that this is most important, other and more urgent injuries than those of the nose were present and owing to the immediate necessity of treating these injuries the condition of the nose and the nasal passages could not be determined in the early stages and was not investigated before discharge from the hospital. For these reasons deflection of the septum and scarring of the wound in the mucosa probably combined to produce a trigger area which, in patients whose nervous balance was disturbed, resulted in the sudden onset of acute asthmatic attacks, which appeared at intervals of from six to eight weeks. The presence of asthma in the two patients was no contraindication to operative treatment. Rapid relief and disappearance of attacks followed surgical intervention. The operation was that of simple resection and the author does not suggest that nasal treatment for asthma of other origin should take this form.

Journal of Laryngology and Otology, London

54: 235-318 (May) 1939

*External Operations on Frontal and Ethmoidal Sinuses. N. Patterson.—p. 235.

Some New Data Concerning Pathology and Treatment of Ozena. G. Hálasz.—p. 245.

Operations on the Sinuses.—So far as the ethmoidal cells are concerned, whether the pathologic change is one of suppuration or polypoid formation or a combination of the two, the common practice has been to attack the disease by the nasal route. However, Patterson asserts that operation on the ethmoidal labyrinth through an external incision is becoming a recognized procedure in cases in which the disease is extensive or when one or more operations by the nasal approach have proved unsuccessful. The two possible objections to the external operation are that it may be more dangerous and that a scar is produced, but operation through an external incision when conditions warrant such a procedure is probably safer than an attempt, and it can only be an attempt, to perform a radical operation by the nasal route. The author states that by employing the method which he describes scarring is negligible. In these "fronto-ethmoidal" cases he relies almost entirely on one or the other of two incisions. The "frontal" incision passes along the supra-orbital ridge and corresponds to the center of the hairy eyebrow or lies just below it. The "ethmoid" incision begins about one-fourth inch below the level of the inner canthus at the upper end of a sulcus or natural fold which can generally be seen passing outward and downward into the cheek. The incision is about 1 inch long. The skin should be sliced—not cut vertically to its surface—by holding the blade of the knife parallel to the skin to be incised. In this way a shelving edge of skin is obtained and when the time comes to close the wound such good apposition is obtained that approximation is very accurate and the resulting scar is generally almost invisible. The author states that the results obtained by the external ethmoid operation are most gratifying. In patients requiring radical treatment an accurate dissection replaces haphazard removal of polyps and bone, which is all that can be accomplished by the nasal route. The patient can be promised a nose permanently free from polyps, and when chronic suppuration is present in the ethmoidal labyrinths excision of the affected area would appear to be the only certain means of eradicating the disease. The author concludes that none of his patients have developed any serious complications and that meningitis need not be feared provided the operation is carried out with care and precision.

Journal of Tropical Medicine and Hygiene, London

42: 97-108 (April 1) 1939

Snake Bites in South Africa, with Special Reference to Their Solid and Grooved Teeth. F. G. Cawston.—p. 97.

Importance of Pathology and Dispensing in Schistosomiasis. F. G. Cawston.—p. 98.

Diseases of Skin in Negroes. L. J. A. Loewenthal.—p. 99.

42: 109-124 (April 15) 1939

*Retrobulbar Neuritis with Pellagra in Nigeria. D. F. Moore.—p. 109.

Retrobulbar Neuritis with Pellagra in Nigeria.—Moore discusses a syndrome that occurs extensively in Southern Nigeria. It consists of perlèche, sore tongue and genitalia and retrobulbar neuritis associated with optic atrophy. The condition has responded dramatically to treatment with autoclaved yeast products and so is believed to be pellagrinous. It is believed that gari, a dried parched manioc food, plays an important part in its incidence. The facts in support of pellagra as the cause of the syndrome in Southern Nigeria are that (1) throughout the palm-oil belt there is an abundance of cheap edible oil, (2) no single case of xerophthalmia has been seen in Southern Nigeria, (3) there is a great relative shortage of animal and fish protein in Southern Nigeria (it is in these areas, or under conditions that permit this shortage, that this syndrome is found) and (4) where gari is eaten to excess in the absence of the protein protective foods it is shown to have an almost constant relationship to the incidence of this syndrome. Gari bears a strong suggestive comparison with "spoiled maize." A nutritional policy based on the recommendations of the League of Nations Health Committee (1937) is required for Nigeria to include particularly the development of local food sources and when possible to abolish by replacement both gari and stockfish as dietary essentials of the people.

Lancet, London

1: 969-1022 (April 29) 1939

Infantile Diarrhea. J. M. Smellie.—p. 969.

*Specific Immunity in Acute Staphylococcic Osteomyelitis with Some Observations on the Causation of Pyemia. F. C. O. Valentine and E. C. B. Butler.—p. 973.

Fixation of Osteo-Arthritic Hip by Nailing. B. H. Burns.—p. 978.

Nail Fixation of Osteo-Arthritic Hip Without Exposure of Joint. E. T. Bailey and H. J. Burrows.—p. 980.

*Primary Peritonitis in Scarlet Fever Treated with Sodium Salt of Sulfapyridine. H. S. Banks.—p. 983.

Specific Immunity in Osteomyelitis.—Valentine and Butler have tried to follow the development of specific antibodies in the serum in cases of acute staphylococcic osteomyelitis and to correlate the results with the clinical severity of

the infection, the persistence of bacteremia and the outcome of the disease. Since there is no reason to suppose that β-hemolysin is of importance in human infection, attention has been concentrated on the α-hemolysin, leukocidin and their antitoxins and on the agglutinin. The cases described include seven cases of acute osteomyelitis in which survival occurred, two of fatal pyemia associated with osseous infection and one of pyemia with no osseous involvement. The study shows that in response to deep-seated staphylococcic infection in man the spontaneous production of antileukocidin bears a close relation to the severity of the clinical condition. No evidence has come to light suggesting that antihemolysin (α) is likely to be of much value in treatment during the acute stage of the infection. There is some indication that the disappearance of staphylococci from the blood stream in acute osteomyelitis may often coincide with the appearance of agglutinins in the serum. In at least two cases, those in which there are pelvic lesions, there was evidence of continued spread of local infection after an apparently satisfactory level of general immunity was established. It is hoped that by improving the general condition of the patient in the first week by the use of antitoxin the resistance of the tissues at the site of infection may be increased. Pyemia is the result of septic venous thrombosis, which may occur either in association with the osseous lesion of osteomyelitis or with a superficial, apparently minor, focus. It is suggested that such a minor focus may in some cases be the main source of bacteremia and of any further lesions which may develop in the course of the illness.

Primary Peritonitis in Scarlet Fever.—Banks reports a case of hemolytic streptococcus septicemia and general peritonitis which occurred on the twenty-sixth day of scarlet fever and was associated with infra-orbital cellulitis, cervical adenitis and nephritis. The patient had not had the benefit of antitoxin treatment in the initial stage of the scarlet fever but had been treated with sulfanilamide, which was badly tolerated. For the peritonitis, since there was no evidence of an abdominal focus, operative treatment was not adopted. Treatment, at first with sulfapyridine by injection of the 20 per cent suspension of the drug, later by injection of the sodium salt and ultimately by oral administration, apparently brought about a rapid sterilization of the pus in the abdominal cavity. The subsequent accumulation of peritoneal fluid was removed by repeated aspirations. There was also an associated bilateral pleural effusion. The patient suffered in convalescence from a profound secondary anemia, which did not improve under iron and liver therapy but rapidly improved after two blood transfusions. He made a good recovery. The advantage of injections of the sodium salt of sulfapyridine in the early treatment of this type of case is emphasized.

New Zealand Medical Journal, Wellington

38: 63-138 (April) 1939

Peptic Ulcer: Present Position of Surgical Treatment. B. T. Edye.—p. 71.
Physiology of Water Exchange. E. R. Reay.—p. 79.
Water Balance: Review of Medical Aspects. D. W. C. Jones.—p. 91.
Water Balance in Surgery. C. M. Greenslade.—p. 95.

Practitioner, London

142: 549-676 (May) 1939

General Management of Diabetes Mellitus. E. Spriggs.—p. 549.
Diabetes Mellitus in Childhood and Youth. Priscilla White.—p. 576.
Differential Diagnosis of Glycosuria. E. N. Chamberlain.—p. 588.
Biochemical Examinations in Diabetes and the General Practitioner. R. D. Lawrence.—p. 596.
Surgery in Diabetes Mellitus. J. B. Hunter.—p. 603.
Visceral Symptoms in Emotional States. W. Langdon-Brown.—p. 609.
*Changes in Nails as Aid to Diagnosis and Prognosis. R. C. Low.—p. 627.
Contact Dermatitis. J. H. T. Davies.—p. 636.
Subphrenic Abscess. W. Broadbent.—p. 643.
Prevention of Tetanus and Gas Gangrene. J. S. K. Boyd.—p. 645.
Diet in Health and Disease: XXIII. Weaning and Mixed Feeding. A. G. Watkins.—p. 655.

Changes in Nails as Aid to Diagnosis.—Low maintains that few medical men, when examining a patient, make even a cursory inspection of the nails. Yet a good deal of information can sometimes be obtained from these structures. Their normal growth depends on the general health and they are quick to show changes when that is interfered with. When all the nails of the hands and feet show the same alteration the presumption is that it is due either to a congenital anomaly or, in the absence of any adjacent skin inflammation, to some general condition affecting all the nails through the circulation. When only some of the nails are affected and others are quite normal, a local cause should be looked for such as a recent or remote injury, an infection of the nail itself (as in ringworm) or an inflammation or growth affecting the skin or deeper tissues round the nail. The fact that the nails are affected in any general condition indicates to some extent its severity and so may influence the prognosis. A change in the color of the nails may be diagnostic of leukonychia, trophic nerve disturbances, arsenical poisoning, Addison's disease, argyria, chronic mercurial poisoning and diabetic and other forms of gangrene. Apart from any alteration in color the nails may become altered in shape and size in various ways, as clubbing of the fingers and toes in chronic pulmonary and cardiac conditions. The opposite condition may also occur. The cause of spoon-nail is not known. It may occur in association with nutritional anemias. As most of the persons in whom it occurs are of the highly strung type, the nervous system may play some part in the etiology. Fragility and splitting of the nails are fairly common. Some persons are born with nails which are brittle and tend to split and break off at the free ends. A similar condition may also be acquired by prolonged or frequent contact with chemicals (as in manicuring), especially alkalis. There is also the condition known as egg-shell nail, in which the nail-plate is soft, is semitransparent, bends easily and splits at the end. This particular change has been reported in association with arthritis, peripheral neuritis, leprosy and hemiplegia. A somewhat similar condition also occurs occasionally in late syphilis, producing onychia syphilitica sicca. In this condition all the nails are affected. They are dry and atrophic and tend to split. It may be the only visible sign of syphilis, but the diagnosis can be confirmed by the Wassermann test. Longitudinal striation of the nails is a common condition in adults past middle life. In slight cases it is merely an exaggeration of the normal longitudinal ridges of the nail bed, but in well marked cases it is accompanied by splitting of the nails (onychorrhexis) at the free margins. It is common in persons who are absorbing from a focus of infection at the root of a tooth or in the bowel. In addition to cases due to focal infection, lining of the nails is seen in gout and nervous diseases such as neuritis and hemiplegia. It is also associated with the dry skin and scanty hair of myxedema. Dryness of the skin and lusterless nails showing longitudinal or transverse lining is also seen in cases of vitamin A, B and D deficiencies. Administration of the appropriate vitamins in these cases will restore the nails to normal. A single raised longitudinal ridge running down one nail is the result of a scar at the base of the nail from previous disease or injury. Transverse lines, usually known as Beau's lines, appear on the nails as a result of previous interference with the growth of the nail matrix. If these lines are due to a local inflammatory cause, usually the nails are not all affected. Shedding of the nails may occur in epidermolysis bullosa, after fevers and in extensive cutaneous diseases. Atrophy of the nails is often associated with ectodermic defects such as extreme thinness or absence of scalp hair. Although not necessarily associated with any mental condition, this change in the nails is fairly frequently seen in mentally defective children. It may also be an acquired condition and may follow injuries, scars from disease, frostbite, sclerodactylia, Raynaud's disease, radiodermatitis and syphilis. It also occurs in hyperthyroidism and exophthalmic goiter and has been reported after nerve injuries, in leprosy, tabes dorsalis and syringomyelia and in prolonged debilitating diseases such as cancer. Thickening and hypertrophy of the nails may occur in chronic eczema with hyperkeratosis of the palms and soles, chronic cutaneous disease, ringworm, paronychia, peripheral neuritis, leprosy, tabes and hemiplegia. Pituitary and thyroid dysfunctions may be responsible for a few cases, but in the majority of cases there is no evident cause except want of cleanliness and neglect.

Archives des Maladies de l'Appareil Digestif, Paris

29: 353-472 (April) 1939

Experimental Study on Influence of Vichy Water on Acid-Base Equilibrium of Bile. Chiray, Dieryck and Mme. Dieryck and C. Debray.—p. 353.
Genesis and Diagnostic Value of Urobilin and of Urobilinogen. D. Antitch and R. Rubénovitch.—p. 365.
*Dietetic Treatment of Diabetes by Diet Relatively Rich in Glucides. I. Teleman.—p. 387.

Glucides in Diabetes.—Teleman points out that, although insulin is of great significance in the treatment of diabetes, the diet remains nevertheless the most important factor of the therapy of this disease. The author shows that a diet which is relatively rich in glucides counteracts the subjective symptoms, averts the peril of coma and contributes to the improvement of the metabolism. He compared the results of this diet with other diets. He reports three cases in which different types of diets were used. A man aged 62 complained of severe headaches and other diabetic symptoms. He had received insulin and a diet in which the carbohydrate intake was restricted to from 80 to 100 Gm. but which had high fat and protein contents. The diet suggested by Porges and Adlersberg provides 300 Gm. of carbohydrates and small amounts of fats and proteins (60 Gm. of each). The patient followed this regimen for three weeks and under its influence the subjective symptoms disappeared, his general condition was much improved and the glycemia and the urea content were less than with the other diet. After the patient had returned for a month to the old diet with restriction of the carbohydrates, tests revealed a renewed increase in glycemia and in the urea content and the general condition was greatly impaired. Convinced of the superiority of the diet with the high carbohydrate content, the patient thereafter voluntarily resumed it. After reporting two similar cases, the author discusses the theoretical foundations of this diet with the high carbohydrate content. He stresses that sugar is an indispensable food for which the diabetic patient has the same need as has the normal person and that care must be taken that the intake and utilization of carbohydrates is sufficient and compatible with the nutritive equilibrium. The essential characteristic of diabetes is a blockage of the utilization of the glucides because of a lack of insulin, which produces cellular hunger by exhaustion of the glycogen in the tissues. The augmented glycemia and the glycosuria must be regarded as compensatory phenomena; they reflect the gravity of the disease but are only secondary symptoms. The treatment of diabetes mellitus must have as its principal aim the enrichment of the organism in utilizable glycogen with the aid of carbohydrate foods. The quantity of calories administered to a diabetic patient should be reduced to a minimum compatible with the nutritive equilibrium and the conservation of a normal weight. The different types of nutrient substances must be apportioned in accordance with the severity of the disorder and the weight of the patient. In the mild forms of diabetes mellitus which do not require insulin therapy, the glucides and proteins should amount to 40 per cent each and the fats to 20 per cent; in the grave forms in which insulin must be given, the glucides should represent 50 per cent, the proteins from 20 to 30 per cent and the fats 20 per cent.

Bruxelles-Médical, Brussels

19: 840-867 (May 7) 1939

Symptomatology of Chronic Tophaceous Gout. F. Francon.—p. 840.
*Present Status of Prophylaxis of Sudden Death by Pulmonary Embolism. J. Rouffart-Marin.—p. 845.

Pulmonary Embolism.—Rouffart-Marin shows that a knowledge of the mechanism of the sudden death by embolism will permit a more effective treatment and will aid in the prevention of this grave postoperative complication. Citing the various anatomic lesions of pulmonary embolism that are detected on necropsy, the author directs attention to the disproportion which often exists between the anatomic lesion and the serious disorder which they provoke; that is to say, a small clot may cause sudden death. The diagnosis of postoperative embolism may prove simple and yet there are some authors who consider it difficult, and experienced surgeons have been known to make erroneous diagnoses of postoperative embolism. Bardin introduced beads into the external jugular vein and found that beads of extremely small caliber which are incapable of impeding the circulation may cause sudden death and he was able to prove that it is the result of a nervous reflex elicited by the embolizing particles on the nervous terminations of the pulmonary arteries. Bardin's observations demonstrated the importance of the sympathetic nervous system in the pathogenesis of postoperative embolism and the prophylactic value of neurosympathetic medicaments. After mentioning other investigators who studied this problem, the author says that he observed thirteen cases of grave pulmonary embolism with ten deaths. After reviewing these cases, he discusses the treatment. He says that in one case he decided to try Trendelenburg's operation but the patient died before it could be carried out. About the medical treatment he says that in the cases which are referred to as grave pulmonary embolism, and which in reality are only pulmonary shock, the therapy must be based on the clinical symptomatology. For cases of embolism of the syncopal form he recommends artificial respiration, oxygen therapy, ephedrine and atropine; for the anginal form morphine, heroin, papaverine, atropine and stellate anesthesia; in the asphyxial form papaverine, sympathicomimetics, respiratory analeptics and oxygen; in collapse, sympathicomimetics, epinephrines, ouabain and respiratory analeptics; in infarct, heroin, papaverine and so on. The peripheral vascular analeptics must be given in large doses. Moreover, the action of these medicaments is favored by the intravenous injection of sodium bicarbonate. In the syncopal form with cardiac arrest, the author was able to save the life of several patients by the intracardiac injection of caffeine, a camphor preparation, epinephrine and atropine. The author further stresses the importance of certain prophylactic measures.

Journal de Médecine de Lyon, Lyons

20: 281-318 (May 5) 1939

*Rapidly Fatal Encephalitides in Children. C. Gardère, M. Dauvergne and G. Bertrand.—p. 281.
Encephalic Metastases and Cerebral Tumors. J. Dechaume, P. Wertheimer and L. Mansuy.—p. 287.
Mematologic Memorandum for Diagnosis and Prognosis of Pulmonary Tuberculosis. Vincenti and Gaussen.—p. 303.

Rapidly Fatal Encephalitides in Children.—Gardère and his associates point out that certain acute encephalitides in children are noteworthy for their particularly rapid development and their exceptional gravity. The encephalitides with rapid death are those in which the evolution does not go beyond the third day. This form seems to appear especially in nurslings. Of forty-three cases, seventeen concerned infants of the first year, nine of the second year and the other seventeen concerned children between the ages of 2 and 12 years. This encephalitis with rapid death is most frequently of the para-infectious type (thirty-four of forty-three cases). Whooping cough seems to be the most frequent causal infection during the first two years of life, and measles during the later years. Varicella and vaccinia are less often the cause. Some cases seem to be primary and their cause is still obscure, but at times they may be of influenzal origin and in other cases a connection with lethargic encephalitis may be considered. The symptomatology is characterized chiefly by convulsions, somnolence and coma. But what is especially characteristic for these forms is the almost immediate appearance of symptoms indicating bulbar involvement: irregularity of the respiratory rhythm and tachycardia. Lumbar puncture usually yields a normal cerebrospinal fluid or one with slight lymphocytic reaction. After reporting six cases the authors discuss the pathologic anatomy. The anatomopathologic studies are as yet few in number but they reveal the usual diffuse lesions of encephalitis with involvement of the bulbar centers, where cytologic lesions are found in spite of the rapidity of evolution. The diagnosis is especially difficult in the primary forms. In nurslings the possible existence of a suppurating otitis or of a mastoiditis must be considered, for these may produce a similar symptomatology. The outcome of the peracute forms of encephalitis is usually rapidly fatal, although occasionally the bulbar symptoms subside and the child recovers.

Riforma Medica, Naples

55: 669-708 (May 6) 1939. Partial Index

Protamine Zinc Insulin in Treatment of Diabetes Mellitus. G. Camerini. —p. 671.
*Bronchography in Diagnosis of Primary Cancer of Lung. C. Scarinci and F. Vitagliano.—p. 680.

Bronchography in Diagnosis of Pulmonary Cancer.—Scarinci and Vitagliano call attention to the importance of the roentgenologic examination of the lung and bronchi for an early diagnosis of primary cancer of the lung. The examination includes (1) radioscopy, (2) roentgen examination of the lung and (3) bronchography under radioscopic control. The latter is the most important phase of the roentgenologic examination of the structures. It is done with the purpose of ascertaining the presence of bronchial stenosis, which is constant in all cases of cancer of the lung, early in the development of the disease. In making radioscopic bronchography the following technic refinements are of importance: (1) inducing a perfect anesthesia to prevent coughing, (2) introducing the iodized oil through an intratracheal sound as far as possible into the bronchi and (3) injecting the oil slowly and under radioscopic control. The posture of the patient during the examination varies with the location of bronchial stenosis (as suspected from the results of the examination of the thorax and by previous radioscopy and the roentgen examination of the lung). According to the authors, radioscopic bronchography is of more diagnostic value than bronchoscopy in cancer of the lung. The value of bronchoscopy is limited to the diagnosis of cancer when it is located in lobes of the lung which correspond to bronchi which are accessible to bronchoscopic examination and not otherwise. A diagnosis of cancer in the upper lobe cannot be made by bronchoscopy. The entire bronchial tree and the points at which the opaque substance stops from stenosis can be seen during radioscopic bronchography. Moreover, an early diagnosis of cancer of any lobe at any distance from the hilus, and either in the lung, the bronchi or the bronchiole, can be done by radioscopic bronchography. Bronchial stenosis shows diminution (or complete closure) of the lumen of a given bronchus by either intrabronchial cancer or by external tumoral compression. When it is present in association with some other clinical symptoms of cancer of the lung, it is a diagnostic sign of almost absolute value. The authors emphasize the diagnostic significance of bronchography, especially because of the fact that cancer of the lung can be controlled (according to the literature) without any recurrences by early surgical operation (exeresis of the involved lung or pneumonectomy). They report two cases of cancer of the upper and lower lobes, respectively, in which the diagnosis was made by radioscopic bronchography.

Archiv für Psychiatrie und Nervenkrankheiten, Berlin

109: 649-847 (April 15) 1939. Partial Index

Atrophy of System of Brachia Pontis and of Inferior Olivary Bodies. E. Welte.—p. 649.
Ocular Symptoms in Patients Who Have Been Treated with Metrazol and Insulin Shock Therapy. V. Čavka.—p. 721.
*Malignant Exacerbation of Multiple Sclerosis. A. Juba.—p. 727.
Behavior of Brain Following Injection of Gold Salts. W. J. Roberts.—p. 744.
Investigations on Pathogenesis of Syphilitic and Tonic Pupillary Disturbances. E. H. Romberg.—p. 785.
Demonstration of Cerebral Deformities by Roentgenogram and Its Clinical Significance. A. Bannwarth.—p. 805.

Malignant Exacerbation of Multiple Sclerosis.—Juba thinks that for the clarification of the relations between multiple sclerosis and encephalomyelitis disseminata, as far as this is morphologically possible, those cases of multiple sclerosis are especially suited in which death resulted from a peracute exacerbation. He describes three microscopically verified cases of multiple sclerosis in which, after a chronic or intermittent course, a peracute exacerbation set in. Death followed in the first case after thirteen days, in the second after seventeen days and in the third after five days. In the first case, of hemiplegia, the anatomic examination disclosed in the medullary substance of the hemispheres many perivascular, encephalomyelitic foci with indefinite outlines. Formation of glia could be observed in a young focus of the wall of the lateral ventricle. In the second case, of tetraplegia with spastic and bulbar symptoms, a sharply defined, new destruction of the medullary substance was demonstrable in the upper cervical section and in the closed oblongata. In the third case the spastic paraparesis was suddenly transformed into a flaccid paralysis; in the anterior horns of the spinal cord, sharply defined, symmetrical foci were found, the central portion of which had broken down. As common characteristics of the acute process the author detected the formation of glial foci around the vessels and around the fluid space with special affinity for the white substance; at any rate, the ganglion cells remained relatively free. As far as the morphologic aspects are concerned, there are doubtless close relations to encephalomyelitis disseminata. Especially characteristic is the rapid growth of the foci, so that the process is not restricted to the juxtavascular region but penetrates deep into the parenchyma; then there is the sharp demarcation and the severe inflammation, which together give a characteristic aspect to the acute phase of multiple sclerosis. If these characteristics are accepted as criteria of the acute phase of multiple sclerosis, and if the morphologic aspects of the cases of encephalomyelitis disseminata are considered, it seems probable that there is a form which belongs to the group of multiple sclerosis and is an especially malignant type of multiple sclerosis. On the other hand, there are cases which have no connection with multiple sclerosis and which, as regards their structure, closely resemble the para-infectious encephalomyelitides. About the pathogenesis the author says that he adheres to the inflammatory character of multiple sclerosis. He admits that the foci usually form around the vessels but says that they also form around the fluid spaces. He does not share Putman's theory of the causal significance of circulatory disturbances and especially of the formation of thrombin in the small vessels; Juba neither detected thrombi nor observed that the process was restricted to the perivascular region.

Klinische Monatsbl. f. Augenheilkunde, Stuttgart

102: 465-608 (April) 1939. Partial Index

*Pathogenesis and Involution of Cataract of Diabetes Mellitus. M. Bücklers.—p. 465.
Operation of Cataract with Scleral Suture. B. von Horváth.—p. 473.
Postoperative Hemorrhage After Extraction of Cataract and Its Causes. F. W. Meyer.—p. 479.
Keratitis Superficialis Punctata. Zur Nedden.—p. 487.
Epidemic of Keratoconjunctivitis Nummularis. H. Schwitalla.—p. 491.
Is Ulcus Corneae Rodens Due to a Deficiency in Vitamin B_1? J. Suurküla.—p. 500.
Local Hyperthermia in Treatment of Ophthalmoblenorrhea. Ida Czukrász.—p. 512.
Large Hemorrhages of Vitreous Body Caused by Retinal Tears. A. Vogt.—p. 516.

Cataract of Diabetes Mellitus.—Bücklers describes his observations in a case in which changes in the lenticular turbidity were recorded continuously and metabolic tests were made simultaneously. A tabular report indicates the gradual retrogression of the cataract, the sugar content of the urine and blood, the specific gravity of the urine, the water balance and the dose of insulin that was administered. The retrogression of the turbidity of the lens began in the axis and advanced in an irregular manner toward the periphery, but it seemed to be more rapid on the temporal side. The table discloses that the subsidence of the turbidity was already noticeable at a time at which there still existed a considerable metabolic disturbance. One increase in the blood sugar was accompanied by a slight increase in the turbidity of the lens, but a second increase in the sugar content caused no lenticular changes. It cannot be decided whether the decrease in the visual acuity was caused by a lenticular turbidity or by a change in the refractive power during the temporary hyperopia. The author believes that the two processes developed simultaneously. In trying to find an explanation for these two disorders, the author cites the theory advanced by Granström for the development of the diabetic impairment in the refraction and the one advanced by Braun for the pathogenesis of the lenticular turbidities. Both of these authors ascribe great importance to the disturbance in the mineral and water exchanges. The turbidity in the lens as well as the transitory hyperopia are apparently due to a temporary increase in the water content of the lens.

Klinische Wochenschrift, Berlin

18: 589-628 (April 29) 1939. Partial Index

Interferometry and Complement Fixation. J. Jochims.—p. 594.
Increase of Lactic Acid and Ketone Bodies in Blood During Intensive and Unaccustomed Physical Work. H. Winkler and F. Hebeler.—p. 596.
Oxygen Consumption of Urine and Oxygen Pressure of Kidney. C. Schlayer.—p. 598.
Substitutional Action of Fetal Adrenals During Pregnancy of Adrenalectomized Dog. F. Billmann and R. Engel.—p. 599.
*Hormone of Ovum. E. Klar.—p. 600.
Question of Etiology of Paroxysmal Paralysis. H. C. à Wengen.—p. 602.
Electrical Studies on Pharmacologic Localization in Brain. Z. Drohocki and Jadwiga Drohocka.—p. 606.

Hormone of Ovum.—Klar says that it is generally assumed that the cyclic changes of the uterine mucosa take place under the influence of estrogen and progesterone and that menstruation sets in as the result of a sudden decrease in progesterone, which in turn is caused by the death of the corpus luteum. This sudden death of the corpus luteum as yet has found no satisfactory explanation. The fact that the corpus luteum is destroyed only when the ovum is not fertilized suggests that the ovum plays an active part in the onset of menstruation. It seems likely that the resorption of the dead ovum liberates hormonal substances, which cause the death of the corpus luteum and thus the onset of menstruation. Whether the dead or dying ovum influences the female sexual cycle has been answered neither positively nor negatively. To determine the endocrine action of the dying ovum, the author made experiments with an extract of fish roe and with extracts of the urine of menstruating women (collected urine of the first day of the menstrual flow). Assuming that the production of abortion in pregnant mice would be a simple test method, the author made experiments on pregnant mice. These revealed the presence of a substance which elicits abortion, apparently as the result of premature detachment of the placenta, during all stages of gestation. The length of time that is required for the elicitation of the abortion is dependent on the dose. This time factor makes possible the quantitative determination of the required dosage; the quantity that elicits abortion in the pregnant mouse within ten hours after the administration is designated as one mouse unit. The substance was tested also on rabbits and it was found that abortion is caused by approximately 200 mouse units. The author cites factors which indicate that the abortifacient effect of the substance extracted from fish roe is not due to one of the fish toxins. In the summary he stresses the following points: 1. A substance can be extracted from ova which regularly elicits premature birth in mice and rabbits. 2. A substance with the same action can be obtained in many but not in all cases from the urine of menstruating women. 3. On the basis of the chemical behavior it is suggested that the substance in question, which as yet has not been isolated, represents a protein body of a low order. 4. These results make an endocrine action of the dead ovum highly probable.

Münchener medizinische Wochenschrift, Munich

86: 561-600 (April 15) 1939. Partial Index

Cause and Course of Epidemic of Dysentery (Flexner) in Two Regiments. Schad.—p. 564.
*Diagnosis and Treatment of Perforated Ulcer of Stomach and Duodenum. W. Geisthövel.—p. 566.
Experimental and Clinical Studies on Blood Transfusion by Means of Continuous Drip Method. H. Mittelstrass.—p. 570.
Free Interval in Postencephalitic Parkinsonism. H. Bubenzer.—p. 573.
Vitamin C as Anti-Infectious Remedy. K. H. Büsing.—p. 575.
Diagnosis and Therapy of Condition of Exhaustion of Obscure Etiology (Contribution to Problem of Focal Infection). L. Walb.—p. 579.
Experiences with Therapeutic Application of Cyrene, a Synthetic Preparation with Actions of Female Sex Hormone. R. Brühl.—p. 582.

Perforated Gastric and Duodenal Ulcer.—Geisthövel discusses the diagnosis and treatment of gastric and duodenal ulcers. He bases his discussion on observations he made in 100 cases. He thinks that the general practitioner can readily recognize a perforated ulcer on the basis of the anamnesis and the clinical aspects, provided, of course, he sees the patient early enough. If a physician is called only after peritoneal symptoms have already developed, it may be difficult to determine the cause. The question whether the first operation should be conservative or radical has not been definitely decided as yet. The author is of the opinion that, on the whole, it is advisable to try to effect cure in a single operation. In his material the primary resection was performed in twenty-six cases. Most of these patients were comparatively young (average age 34 years) and the operation was nearly always performed in the course of the first six hours after the perforation. In none of the cases in which extensive resection was decided on had more than twelve hours elapsed since the operation. He points out that the mortality increases with the length of the time interval. To be sure, other factors, particularly the patient's general condition and the local aspects, that are detected when the abdomen is opened, are important factors in deciding the type of surgical intervention. Following the evaluation of the palliative resection (resection for exclusion according to Finsterer), the author says that in twenty-four of his patients resection according to the second method of Billroth was done. Billroth's first method was performed in only two of the cases, for this method involves considerable dangers. The author stresses as an advantage of the primary resection that it removes simultaneously the ulcer as well as its cause, the "acid producer," and thus prevents relapsing ulcers and other sequels. If the first operation is a conservative procedure in the form of simple suturing, the secondary resection should be made soon after, because simple suturing is often followed by a new perforation, by stenosis or by cancer. In secondary resections the duration of the operation is usually prolonged as the result of adhesions. The author regards the prophylactic operation of the ulcer as the best treatment. It has been proved by statistics that the duodenal ulcers of the anterior wall perforate most frequently and the prepyloric ulcers have the greatest tendency to malignant degeneration and to penetration into the pancreas. He thinks that these types should be subjected to surgical treatment if, after two or three internal treatments, they have not subsided.

Wiener klinische Wochenschrift, Vienna

52: 393-416 (April 28) 1939. Partial Index

*Juxtacardiac Gastric Ulcer. H. Finsterer.—p. 394.
Treatment of Vomiting in Pregnant Women. H. Kutschera-Aichbergen.—p. 400.
Bilateral Cystic Kidney: Case. E. Rissel.—p. 401.

Juxtacardiac Gastric Ulcer.—Finsterer maintains that the juxtacardiac ulcers hold a special position not only because of their relative rarity but also because their diagnosis and treatment are rather difficult. In a critical analysis of the results which he obtained in the surgical treatment of juxtacardiac ulcers he finds that the mortality rate was comparatively high in his material because, in some difficult cases in which the resection of the ulcer was forced, Madlener's operation should have been made. To reduce the acidity in juxtacardiac ulcers, Madlener removes the distal half of the stomach together with the pylorus but leaves the ulcer untouched and makes the anastomosis with the duodenum according to the first method of Billroth. Finsterer says that in the future he intends to resect the ulcer only if by gastrotomy and by intragastric palpation it has been determined that the ulcer is far enough removed from the esophagus that a secure closure of the gastric stump can be obtained. For all other cases he recommends Madlener's operation, which permits a reduction in the surgical mortality and also insures better permanent results than does simple gastro-enterostomy. The latter method should be employed only in exceptional emergencies. The author thinks that in the interest of the patients it is better to perform Madlener's resection too often than not often enough in cases of juxtacardiac gastric ulcer.

Novyy Khirurgicheskiy Arkhiv, Dnepropetrovsk

42: 227-352 (No. 167) 1939. Partial Index

Acute Intestinal Obstruction in Children. V. P. Voznesenskiy.—p. 227.
*Late Results and Recurrent Manifestations Following Operations for Cholecystitis and Its Complications. A. G. Sosnovskiy.—p. 247.
Clinical Value of Venography. Ya. I. Arkusskiy.—p. 280.
Metaphen Treatment of Wounds. V. I. Rozhanskiy and I. V. Kamenskaya.—p. 287.
Immunobiologic Features of Chronic, Suppurative Processes. I. S. Kogan.—p. 292.

Late Results After Cholecystectomy.—A follow-up study of 400 patients operated on at the Medical Institute of Odessa, according to Sosnovskiy, revealed a complete clinical recovery in 82.5 per cent, improvement in 12 per cent and failure to

improve in 5.5 per cent. Recurrent manifestations were present in 4.2 per cent after operations for uncomplicated cholecystitis, in 18 per cent after operations for cholecystitis with complications of medium severity and in 34 per cent after operations for cholecystitis associated with severe complications. Recurrence of pain was present in 25.5 per cent of all cases. In 8 per cent there was pain which lasted for from one and one half to five months and was followed by a complete clinical recovery; in 12 per cent the pain recurred for a period of from one half to three years and was followed by considerable improvement, while in 5.5 per cent pain was present for from three to eleven years and there was no improvement in the clinical condition of the patient. The author concludes that an early and timely operation when the inflammatory process is localized in the gallbladder and does not involve the adjacent viscera is essential to the obtaining of satisfactory late results. Cholecystectomy is the operation of choice in cholecystitis. It results in a small mortality rate and is rarely followed by a recurrence. Choledochotomy with drainage of the hepatic or the common bile duct is indicated in obstruction of the bile passages complicated by cholangitis, hepatitis or pancreatitis. Drainage of the duct may be omitted on the removal of the obstruction, in the absence of complications and with a patent papilla of Vater. Cholangitis, hepatitis and pancreatitis were the more frequent causes of recurrence. In the majority of the cases these causes were associated with one another. Among the less frequent conditions the author lists stones overlooked at the time of operation, strictures and obliteration of the deep biliary ducts, dyskinetic disturbances and adhesions. Operation undertaken for stasis gallbladder is seldom followed by relief in view of the fact that stasis of bile is brought about by dyskinetic disturbance, the treatment of which is essentially conservative. Because of multiplicity of factors the exact cause of a recurrence cannot be easily ascertained in most cases. Aspiration of duodenal contents, mineral waters, physical therapy, mud baths, a dietetic regimen, nupercaine hydrochloride blockade after Speranskiy, infiltration of Head's zones, and psychotherapy are the therapeutic measures first to be tried in the treatment of recurring manifestations. A secondary operation is indicated when conservative measures fail and when indications of a stone in the choledochus, of a stricture of a duct or of adhesions in the vicinity of the gastric antrum or the duodenum are present. The author concludes that the problem of prevention of recurrences after cholecystectomy depends on unanimity between surgeons and internists as to operative indications. Only an early and timely operation is capable of further reducing the mortality rate and the incidence of failures.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

83: 1709-1816 (April 15) 1939

Genital Hemorrhages During Climacteric. M. A. van Bouwdijk Bastiaanse.—p. 1710.
Influence of Splenectomy on Course of Guinea Pig Test of Cutaneous Tuberculosis. P. H. J. Lampe.—p. 1718.
Prontosil and Agranulocytosis. C. L. H. Majoor.—p. 1725.
*Quick's Test of Hepatic Function. G. A. Lindeboom.—p. 1734.
Medicinal and Dietetic Treatment of Infections of Urinary Passages. J. G. G. Borst.—p. 1739.
Malignant Leiomyoma of Uterus with Large Cardiac Metastasis: Case. P. H. Hartz and A. van der Sar.—p. 1746.

Quick's Test of Hepatic Function.—Lindeboom directs attention to a test of the hepatic function which was first suggested by Quick and was described in the *American Journal of the Medical Sciences* **185:**630 (May) 1933 (abstracted in THE JOURNAL Sept. 2, 1933, page 101). The test is based on the secretion of hippuric acid following the administration of sodium benzoate. The author found that the test reveals disturbances not only in renal diseases with nitrogen retention but also in many hepatic disorders such as obstructive jaundice, cardiac engorgement of the liver, hepatitis and cirrhosis. He thinks that as yet the test cannot be recommended for routine use in the clinic. Nevertheless it is of theoretical interest that the synthesis of hippuric acid can be employed as an indicator of an impairment of the hepatic parenchyma. Moreover, the test can be used to obtain information about the course of a hepatic disorder. It is also of interest that the test reveals abnormal values in many cases of catatonia.

Acta Medica Scandinavica, Stockholm

99: 511-622 (April 26) 1939

Benign Tuberculoma—Probably Identical with Benign Lymphogranuloma of Schaumann—Causing Bronchial Stenosis. R. Opsahl.—p. 511.
Variations in Uric Acid Clearance After Administration of Purine, with Special Reference to Threshold Problem. K. Brøchner-Mortensen. —p. 525.
*Diagnosis of Gout. K. Brøchner-Mortensen.—p. 538.
*Lymphocytopenia and Fever. F. Sundelin.—p. 563.
Beriberi (Followed by Pellagra), Verified, and Followed During Improvement, by Analyses of Vitamin B_1 in the Blood: Case. J. Lehmann and H. E. Nielsen.—p. 577.
*Fate of Transfused Red Blood Cells. H. J. N. Dekkers.—p. 587.
Sulfanilamide Granulocytopenia. H. Myhre.—p. 614.

Diagnosis of Gout.—Brøchner-Mortensen says that it is well known that during the first twenty-five years of this century the incidence of gout diminished considerably but that during the last few years it has increased again. Even though this change of incidence is unquestionable, the fluctuations are strongly accentuated by simultaneous variations in the nosographic delimitation of the morbid picture. In his paper the author reviews the different diagnostic criteria of gout on the basis of the literature and of his own studies on thirty patients with typical gout. He shows that the anamnesis and the observation of the acute attack are most reliable diagnostic aids. Subcutaneous uratic tophi (verified by the murexide test) are pathognomonic for gout, but they are an inconstant and, in the majority of cases, tardy symptom. Roentgenologically detectable defects resembling tophi in the bones occur earlier and more frequently, but they are not pathognomonic for gout. Hyperuricemia is found in 75 per cent of the cases, being an almost constant symptom when the disease has existed for some years, but it may be conjoined with other disorders. The endogenous excretion of uric acid is normal in cases of gout. The renal function measured with the creatinine and urea clearance is normal in the majority of the cases. There is no relative reduction of the uric acid clearance as compared to the creatinine and urea clearance. After intravenous or oral administration of purine an increase of the uric acid clearance amounting to at least 50 per cent, and often more, is found in normal persons. In patients with gout, a less marked increase of the uric acid clearance is generally found, but in some cases the reaction after administration of purine is found to be normal. Attempts at provoking acute attacks by administration of a diet rich in purine or of a ketogenic diet for a prolonged period as a rule gave negative results. After a ketogenic diet the uric acid excretion is found to be reduced but the renal function on the whole is not changed. Mostly, though not always, the sedimentation rate of the red blood corpuscles increases during an acute attack of gout. Examination of the blood picture revealed polycythemia in three patients. Fourteen of the thirty patients with gout were found to have a slight impairment of the hepatic function or lesions of the hepatic parenchyma. The author examined cases in which the diagnosis of atypical gout had been considered. However, none of these cases afforded a clue which would justify this diagnosis. Anamnesis and articular symptoms were not typical. Hyperuricemia and true tophi were absent. Exogenous administration of uric acid gave normal reactions. On the other hand, defects resembling tophi in the bones were found in several cases. Nevertheless the author is of the opinion that, theoretically, the occurrence of atypical cases cannot be excluded.

Lymphocytopenia and Fever.—During the treatment of rheumatoid arthritis with gold salts, Sundelin observed transient lymphocytopenia. This lymphocytopenia, which in the majority of cases was severe, made its appearance some few hours after the injection and was accompanied by a feeling of malaise, poor general condition, high fever and a number of other symptoms. After some hours, at most after twenty-four hours, the acute

symptoms disappeared and the blood picture regained its normal appearance. The question arose whether the gold salts caused the lymphocytopenia or whether it was simply a symptom accompanying the fever. To throw light on this problem the author made experiments with artificially induced fever. In thirty-five persons fever was produced with injections of various types of vaccine, in two with protein injections, in four with injections of sulfur and in seven with hot baths and packs. Studies were made also on two patients with sepsis and on two patients undergoing malaria therapy. In the summary the author says that his material is too small to permit generalizing conclusions, but he thinks that it is sufficiently large to establish that the transitory extreme lymphocytopenia which appears first after unspecific fever therapy and secondly in other fever conditions is a biologic reaction which, on the whole, runs inversely congruent to the fever. Theoretically the observation gives rise to questions about the origin of the lymphocytes, their task and fate, and, last but not least, the central nervous regulating mechanism by which both the morphologic and the chemical constituents of the blood appear to be controlled.

Fate of Transfused Erythrocytes.—Dekkers shows that there is no general agreement about the length of time for which the transfused erythrocytes remain in the circulation of the recipient. The survival time given in the various reports varies between eight hours and 100 or more days. This divergence in opinion is chiefly due to the fact that the transfused erythrocytes could not be detected directly in a specimen of blood, withdrawn after transfusion, and studies had to be made mostly with indirect methods. By means of the "hetero-agglutination factors" M and N described by Landsteiner and Levine, the direct detection of the transfused red blood corpuscles became possible. Using this improvement the author followed the fate of the transfused erythrocytes in thirty-two patients. In all, thirty-five transfusions were given to these thirty-two patients. The method used by the author makes it possible to detect the erythrocytes of the donor by means of "direct differential agglutination tests" which use M and N test fluids. The cases were selected in such a way that the erythrocytes of the donor contained a factor (M or N) which the erythrocytes of the recipient did not possess, donor and recipient belonging to the same iso-agglutination group. On the basis of his studies the author arrives at the following conclusions: 1. The described method is suitable for the determination of the length of survival of transfused erythrocytes. 2. The transfused cells could be observed for a considerable time. They disappeared gradually from the circulation of the recipient. 3. In cases in which 500 cc. of blood was transfused and an unfavorably acting factor from the side of the recipient could be excluded, the average time during which the erythrocytes of the donor were detectable was from fifty-four and one half to seventy-five and one half days. 4. The following factors appeared to influence this time: (*a*) the normal time of existence of human erythrocytes, (*b*) the quantity of transfused blood and (*c*) the condition of the recipient. An unfavorable influence was seen in a patient suffering from hemolytic jaundice. 5. No sensitization occurred in the first four or five transfusions with blood containing a hetero-agglutination factor. 6. In the treatment of serious acute and chronic anemias, transfusion of blood is by far superior to infusion of other fluids. 7. Although the time of survival of human erythrocytes could not be determined exactly with this method, the results of these investigations give evidence that it is much longer than is generally assumed; it may be three months and more.

Nordisk Medicin, Helsingfors

2: 1147-1226 (April 22) 1939

*Extrapleural Pneumothorax, With Special Reference to Cases of Pulmonary Tuberculosis Regarded as Not Able to Bear Thoracoplasty. J. Holst and E. Refsum.—p. 1147.

Extrapleural Pneumothorax.—Holst and Refsum performed extrapleural oleothorax or pneumothorax on thirty-eight patients too weak to allow other treatment. One patient died three weeks later, perhaps as an indirect result of the operation. One died thirty-two days after the operation from mixed infection and progression of the tuberculous process. Of the twenty-two patients treated for from two to ten months, thirteen are for the time being abacillary, with obliteration of the cavity. The authors find the results encouraging but do not at present consider extension of the indications justified, as the material is too small and the time of observation not long enough for evaluation of the uncertain factors, chief of which is the danger of infection.

Hospitalstidende

*Subacute and Chronic Myocardial Lesions Due to Blunt Traumas. E. Warburg.—p. 1157.

Myocardial Lesions Due to Trauma.—Warburg says that there is no form of myocardial insufficiency or of symptoms from the heart musculature on the whole which cannot be caused by nonpenetrating trauma. Arteriosclerosis and hypertension were predisposing factors in at least eleven of the thirty-eight cases discussed. As a rule the trauma was localized to the thorax. A latent period of several days may elapse between the trauma and the appearance of grave symptoms from the heart. In one instance several months passed before more marked symptoms set in. A varying electrocardiogram is of great value in the diagnosis of traumatic disturbances of the heart musculature, and a persisting abnormality of the electrocardiogram is also of interest; almost every known electrocardiography anomaly, except some rare arrhythmias, occurs in the material. The electrocardiogram may be normal. In some cases recovery takes place after a few weeks; in numerous cases a chronic heart insufficiency develops which more or less rapidly leads to death. Of the thirty-eight patients nine died, seven of these from ten days to two years after the trauma. Patients with heart lesions due to blunt trauma, the author says, are treated in the same way as other patients with disorders of the heart musculature. The large number of traumatic coronary occlusions confirm his earlier view that these heart lesions should not be treated operatively.

Norsk Magasin for Lægevidenskapen

World View of Diabetes Mellitus. E. P. Joslin.—p. 1173.
*Angina Pectoris with Xanthomatosis: Hereditary Disease. C. Müller. —p. 1183.
Weil's Disease Due to Rat Bite. C. H. Bie.—p. 1191.

Angina Pectoris with Xanthomatosis.—Müller says that xanthomatous heart disease is frequent and reports seventeen families in which heart disease due to xanthomatosis was inherited as a dominant factor. In ten of the families there was angina pectoris and xanthoma tuberosum alone or in combination with xanthelasma, in six angina pectoris and xanthelasma, in three angina pectoris without xanthoma or xanthelasma but with other conditions pointing to xanthomatosis as an essential cause. Of the seventy-nine persons included, thirty-five were examined personally. Xanthomatosis causes a special form of arteriosclerosis distinguishable etiologically and clinically from the usual arteriosclerosis. While the xanthomatous deposits may cause valvular defects, they far more often lead to changes in the coronary arteries with angina pectoris. Cardiac disorder may appear in young persons but is more often seen in middle-aged and old persons. It may be chronic and long continued or may cause sudden death. Symptomatologically this form of angina pectoris does not differ from the usual form. Heart infarct is common. Hypercholesterolemia, established in all of the cases examined, was highest in those in which xanthoma tuberosum existed. There was no regular relation between the changes in the skin and the degree of hyperchlosterolemia. Hypertension was rare. Both xanthoma tuberosum and xanthelasma are sometimes so little prominent that they may easily be overlooked on clinical examination. Confusion with other diseases of the skin may also occur. In hereditary heart disease in which rheumatic fever, syphilis and hypertension are excluded, xanthomatosis should be borne in mind as the possible cause. Müller prescribes diet deficient in cholesterol and thyroid tablets for his patients, without to date having been able to form any certain idea as to the effect, and thinks that this treatment may also conceivably be of prophylactic value for the predisposed but not yet affected members of xanthomatous families.